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SPREAD OF THE EPILEPTIC DISCHARGE

AN EXPERIMENTAL STUDY OF THE AFTER-DISCHARGE INDUCED BY ELECTRICAL STIMULATION OF THE CEREBRAL CORTEX

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The purpose of this communication is to report on original experiments concerned with the spread of the epileptic discharge produced by electrical stimulation of the monkey's cerebral cortex. By epileptic discharge is implied the excessive, violent activity of certain portions of the central nervous system which is responsible for many, if not all, of the manifestations of epileptiform fits and epilepsy. This hypothesis invoking excessive function of the gray matter of the cerebral cortex, as expressed by Hughlings Jackson, has received much support in recent investigations on epilepsy. There is ample evidence that the after-discharge produced by stimulation of the cerebral cortex in monkeys is a satisfactory experimental counterpart of epilepsy in man.

Available to the investigator of today are four methods by which to gain information concerning the spread of the epileptic discharge. The first is by observing the march of clonic movements, following the order in which different parts are affected one after another. The second is by recording the local changes in blood flow of the brain which have been shown recently to occur with increased neuronal activity. The third is by following the changes in electrical activity in different regions of the brain as they are activated by the epileptic process. A fourth method, which I have not used, may be to follow the local changes in the p_H of the cerebral cortex. The literature will be briefly reviewed according to the methods which have been utilized by various authors in approaching the problem.

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REVIEW OF LITERATURE

The first study of the focal forms of epilepsy and the manner of their spread was that of Bravais,[1] which appeared as a thesis written for the degree of doctor of medicine from the Faculté de Médecine of Paris. Bravais used the term *marche,* and it is with justice that the French medical profession speaks of *épilepsie Bravais-Jacksonienne.* However, Bravais had no conception of any physiologic basis for the epileptiform fit, and he made no attempt to interpret what he saw. As Jefferson [2] has pointed out in a scholarly article, his intention was to define a variety of epilepsy which he thought is more curable than the generalized sort.

Hughlings Jackson, with his deep insight and philosophic approach, was able to make advances in almost every field of neurology, many of them based on his studies of focal epilepsy and its spread or march, terms which he used interchangeably. As pointed out by Penfield and Gage,[3] the hypothesis that the epileptic discharge may remain localized near its site of origin or may spread topographically to adjacent areas of gray matter over the cerebral cortex, a spread by contiguity, must still be accepted. Although many of Jackson's hypotheses have been verified by later work, it is improbable that he was correct concerning the mechanism of epileptic spread, when he wrote in 1870 [4]:

> It is, I speculate, through the arteries that sequence of movements is developed, whether those movements be spasm passing up the arm and down the leg, or whether they be the orderly sequences of movements in health.

It is probable that Jackson's views on the spread of the epileptic discharge would have been different if he had had available the results of modern studies on cytoarchitectonics and myeloarchitectonics.

There have been relatively few studies on the spread of epileptic activity in the brain. The earlier experimental work on this subject was reviewed and critically analyzed by Karplus.[5] This author, after carrying out studies on both dogs and monkeys, came to the conclusion that local cortical stimulation with a weak electric current would produce a generalized epileptic discharge even after complete longitudinal section of the corpus callosum. He expressed the opinion that this spread occurred by way of corticotegmental pathways to the brain stem.

1. Bravais, L. F.: Recherches sur les symptômes et le traitement de l'épilepsie hémiplégique, Thesis, Paris, no. 118, 1827.

2. Jefferson, G.: Jacksonian Epilepsy: A Background and a Postscript, Post-Grad. M. J. **11**:150-162, 1935.

3. Penfield, W., and Gage, L.: Cerebral Localization of Epileptic Manifestations, Arch. Neurol. & Psychiat. **30**:709-727 (Oct.) 1933.

4. Jackson, J. H.: A Study of Convulsions, Tr. St. Andrews M. Grad. A. **3**: 1-45, 1870; in Taylor, J.; Holmes, G., and Walshe, F. M. R.: Selected Writings of John Hughlings Jackson, London, Hodder & Stoughton, Ltd., 1931, vol. 1.

5. Karplus, I. P.: Experimenteller Beitrag zur Kenntnis der Gehirnvorgänge beim epileptischen Anfalle, Wien. klin. Wchnschr. **27**:645-651, 1914.

Karplus, as well as Spiegel and Falkiewicz, were handicapped by having available only one criterion for the spread of the epileptic discharge, namely, the motor manifestations. Spiegel and Falkiewicz,[6] in a short communication, reported that in dogs generalized convulsions might follow unilateral cortical stimulation even after section of the corpus callosum and all the midline structures. However, after midsagittal section of the pons the convulsion from unilateral cortical stimulation was limited to the contralateral extremities. Later, Spiegel [7] reviewed the literature on this subject and amplified his previous conclusions.

A novel approach to the problem of epileptic spread is that of Penfield and Boldrey,[8] who analyzed atypical cases of stimulation of the epileptic cortex in man. They believe that the responses obtained at a distance from the sensory and motor areas are due to a selective neuronal conduction. Their hypothesis is that continued repetition of an epileptic seizure of a fixed pattern eventually activates a neuron pattern, so that it becomes stimulable electrically, although it was not so under normal conditions.

The fact that local changes in the blood flow through the cerebral gray matter may be used as an index of epileptic discharge has evolved from the many excellent studies on cerebral circulation in recent years. Gibbs [9] and Gibbs, Lennox and Gibbs [10] showed that there is a general increase in blood flow through the brain during a convulsion. Penfield, von Santha and Cipriani [11] have demonstrated that there is a local increase in blood flow in the cerebral gray matter accompanying the epileptiform fit, both in man and in experimental animals, similar to the increased blood flow accompanying increased neuronal activity, as shown by von Santha and Cipriani,[12] Serota and Gerard [13] and others.

6. Spiegel, E. A., and Falkiewicz, T.: Experimentelle Untersuchungen über die Ausbreitung der Erregung im epileptischen Anfall, Klin. Wchnschr. **5**:606-607, 1926.

7. Spiegel, E. A.: Wie kommt es zur Generalisierung der Rindenerregung im epileptischen Anfall? Wien. klin. Wchnschr. **40**:1150-1152, 1927; Central Mechanism of Generalized Epileptic Fits, Am. J. Psychiat. **10**:595-609, 1931.

8. Penfield, W., and Boldrey, E.: Spread of Discharge and Distant Response in the Cerebral Cortex of the Epileptic, Am. J. Psychiat., to be published.

9. Gibbs, F. A.: Cerebral Blood Flow Preceding and Accompanying Experimental Convulsions, Arch. Neurol. & Psychiat. **30**:1003-1010 (Nov.) 1933.

10. Gibbs, F. A.; Lennox, W. G., and Gibbs, E. L.: Cerebral Blood Flow Preceding and Accompanying Epileptic Seizures in Man, Arch. Neurol. & Psychiat. **32**:257-272 (Aug.) 1934.

11. Penfield, W.; von Santha, K., and Cipriani, A.: Cerebral Blood Flow During Induced Epileptiform Seizures, Human and Mammalian, J. Neurophysiol. **2**:257-267, 1939.

12. von Santha, K., and Cipriani, A.: Focal Alterations in Subcortical Circulation Resulting from Stimulation of the Cerebral Cortex, A. Research Nerv. & Ment. Dis., Proc. (1937) **18**:346-362, 1938.

13. Serota, H. M., and Gerard, R. W.: Localized Thermal Changes in the Cat's Brain, J. Neurophysiol. **1**:115-124, 1938.

Apparently, no one, prior to the present study, has utilized these changes as an indicator by which to follow the manner of spread of the epileptic discharge. Kornmüller,[14] principally on the basis of his electroencephalographic researches on the rabbit brain, discussed the mechanism of the epileptic attacks in rabbits and, to a lesser extent, in monkeys. He concluded that activity induced by stimulation of one center may, after a latency of several seconds, spread to other centers via neuronal, and not vascular, pathways.

Adrian and Mathews[15] studied the characteristic sequence of the waves of electrical potential following stimulation of the cortex by local injury, while Adrian[16] investigated the structures responsible for the changes in potential following electrical stimulation. This problem he studied in rabbits under dial anesthesia and found that the simplest response, evoked by weak stimuli, is a change in potential lasting about one-hundredth second, in which the stimulated region becomes negative to points a few millimeters away, though these are positive to points beyond. "This response is due to neurones which are in the superficial layers of the cortex and are all directly excited by the stimulus."

Repeated stimulation with stronger currents brings about a change in the form of the response. The stimulated region now becomes positive to distant points, and the responses become larger and larger as stimulation proceeds. The chief change in potential is now due to elements with the active region some distance below the surface. When the deep response has developed, a wave of potential spreads outward in a circle, owing to conduction of activity from neuron to neuron in the deeper layers.

When the motor area of the monkey is stimulated it is found that the appearance of movements in the limbs is correlated with the appearance of the "deep" cortical response. In after-discharges there is also a spatial and temporal correspondence between the potential waves in the cortex and the movements of the limbs, the stage of clonic movements corresponding to the grouped after-discharge.

Gerard and Libet[17] studied the action of drugs on the potentials recorded from the isolated frog brain. Caffeine initiated powerful diphasic waves that spread over the entire hemisphere. These waves were slowed but not blocked by nicotine.

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14. Kornmüller, A. E.: Die biolectrischen Erscheinungen architektonischer Felder der Grosshirnrinde, Biol. Rev. **10**:383-426, 1935.

15. Adrian, E. D., and Mathews, B. H. C.: The Interpretation of Potential Waves in the Cortex, J. Physiol. **81**:440-471, 1934.

16. Adrian, E. D.: The Spread of Activity in the Cerebral Cortex, J. Physiol. **88**:127-161, 1936.

17. Gerard, R. W., and Libet, B.: Action of Drugs on Potentials of Isolated Frog Brain, Proc. Am. Physiol. Soc., 1939, p. 84.

Gozzano [18] observed that local application of strychnine to one hemisphere produced similar spikes in the electrogram from both hemispheres, a phenomenon which was abolished by section of the corpus callosum.

Dusser de Barenne, McCulloch and Ogawa [19] studied the distribution of the rapid fluctuation in potential, or "strychnine-spikes," produced by the strychninization of only a few (1 to 4) square millimeters of the cerebral cortex. In some regions of the cortex, e. g., the visual cortex, this change remains local; in others the hyperactivity induced by strychnine does not remain confined to the strychninized locus, but spreads.

The areal distribution of these spikes differs with each area locally strychninized, thus revealing details of functional organization, i. e., specifically directed functional (and obviously anatomical) relations, in the sensorimotor cortex.

No "firing" of any area of the arm subdivision was found on local strychninization of any area of the face region, or vice versa.

The studies of Dusser de Barenne, McCulloch and Nims,[20] using a glass electrode to record the hydrogen ion concentration of the cortex, offer another method by which to study the epileptic discharge and its spread.

MATERIAL AND METHODS

Monkeys under light ether anesthesia supplemented with local injections of nupercaine (1: 1,500 solution) were used in this study. The head was fixed rigidly in a holder, but the extremities were suspended through the openings in a hammock designed to permit accurate observation of all convulsive movements. Stimulation was carried out by means of a thyratron stimulator. The duration of the stimulus varied from one-half to twenty seconds, and will be detailed with each experiment. The strength of stimulus has been recorded in arbitrary units, with 10 as a minimum. With a frequency of 60 and an electrode resistance of 5,000 ohms, an intensity of 1 corresponds to 15 volts; of 2 to 20 volts; of 3 to 25 volts; of 4 to 30 volts; of 5 to 35 volts; of 6 to 45 volts; of 7 to 50 volts; of 8 to 60 volts; of 9 to 75 volts, and of 10 to 100 volts.

The recording electrodes were made of 31 gage, annealed silver wire coated with bakelite varnish and exposed for a distance of 0.5 to 1 mm. at the tip. The electrodes were chloridized freshly before each experiment, and proved satisfactory when mounted in an adjustable holder fixed rigidly to the skull. Electrocorticograms were recorded, using a four channel, ink-writing electromagnetic oscillograph with push-pull, condenser-coupled preamplifiers. Standard designations for the

18. Gozzano, M.: Biolektrische Erscheinungen bei der Reflexepilepsie, J. f. Psychol. u. Neurol. **47**:24-39, 1936.

19. Dusser de Barenne, J. G., and McCulloch, W. S.: Functional Organization in the Sensory Cortex of the Monkey, J. Neurophysiol. **1**:69-85, 1938. Dusser de Barenne, J. G.; McCulloch, W. S., and Ogawa, T.: Functional Organization in the Face-Subdivision of the Sensory Cortex of the Monkey, ibid. **1**:436-441, 1938.

20. Dusser de Barenne, J. G.; McCulloch, W. S., and Nims, L. F.: Changes of Hydrogen Ion Concentration of the Cerebral Cortex, Proc. Soc. Exper. Biol. & Med. **36**:462-464, 1937; Functional Activity and p_H of the Cerebral Cortex, J. Cell. & Comp. Physiol. **10**:277-289, 1937.

electrodes have been used in all the protocols and illustrations. The recording electrodes, indicated by Arabic numerals, were connected with the input of the amplifiers, indicated by Roman numerals, as follows: 1 and 2 to amplifier I; 3 and 4 to amplifier II; 5 and 6 to amplifier III, and 7 and 8 to amplifier IV. The Arabic numerals when placed close together on a diagram of the brain indicate bipolar leads, while those placed anterior to the frontal pole indicate monopolar leads. In the latter form the indifferent lead was placed beneath the electrode holder in the midline over the frontal poles. The holder used for the recording electrodes during acute experiments was satisfactory and easily adjustable to all the curvatures of the cortex. An independent but similar holder clamped to the skull was used for the stimulating electrodes. The combination of an electrode holder clamped to the skull and a very light, flexible and pliable silver wire electrode produced a system which was singularly uninfluenced by movement and, at the same time, reduced trauma of the cortex to a minimum. The observations on the blood flow were carried out by the thermoelectric method described by Gibbs,[21] von Santha and Cipriani [12] and others.

The surgical procedures were two: section of the corpus callosum and transcortical section. Section of the corpus callosum was accomplished by clipping one or two cortical veins as they entered the sagittal sinus and usually by clipping the anterior cerebral artery, neither of which procedures interfered with the changes in blood flow or the electrical activity before or during the fit. For a fuller discussion of these procedures the reader is referred to the papers of Watts [22] and Kennard and Watts.[23]

The transcortical sections were made in either of two ways: destruction of a wide area, from 2 to 4 mm., by electrocoagulation or excision, or a simple suture tied together so as to sever the nerve connections but to allow continued coaptation of viable tissue. When this study was begun, it was considered possible that these two methods might have different effects in altering the spread, even though the lesion were of the same linear extent and location. All transcortical sections were made at right angles to the central sulcus, but were of varying depths and of different anteroposterior extents.

RESULTS

The effect of section of the corpus callosum on the spread of the after-discharge has been studied in a total of 14 monkeys, and that of transcortical sections, in another 14 monkeys. Nine cats and 10 dogs were also used for this aspect of the investigation, but did not give satisfactory results, primarily because of the topography of the motor area. Significant illustrative facts are presented from the protocols of various experiments on monkeys, first, from those in which the electrogram was used to study the spread of epileptic activity and, second, from one experiment in which the changes in blood flow were used.

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21. Gibbs, F. A.: A Thermoelectric Blood Flow Recorder in the Form of a Needle, Proc. Soc. Exper. Biol. & Med. **31**:141-146, 1933.

22. Watts, J. W.: Ligation of the Anterior Cerebral Artery in Monkeys, J. Nerv. & Ment. Dis. **79**:153-158, 1934.

23. Kennard, M. A., and Watts, J. W.: The Effect of Section of the Corpus Callosum on the Motor Performance of Monkeys, J. Nerv. & Ment. Dis. **79**:159-169, 1934.

PROTOCOL P2120.—*Macaca mulatta monkey. Electrocorticogram; cortical stimulation; transcortical section.*

With the animal under light ether anesthesia, supplemented with nupercaine (1 : 1,500 solution) injected locally in the scalp, bilateral craniotomy was performed. The cerebral cortex was explored with the bipolar electrodes placed as usual 2 mm. apart, the intensity of the stimulus being 3, the frequency 60 cycles and the duration one-half second. Good focal responses of the leg, arm and face were obtained from the precentral gyrus.

Recording of the electrogram directly from the cortex was then begun with nonpolarizable electrodes placed as usual on the precentral gyrus. Codeine sulfate, ⅛ grain (0.008 Gm.), was given hypodermically after cessation of ether anesthesia.

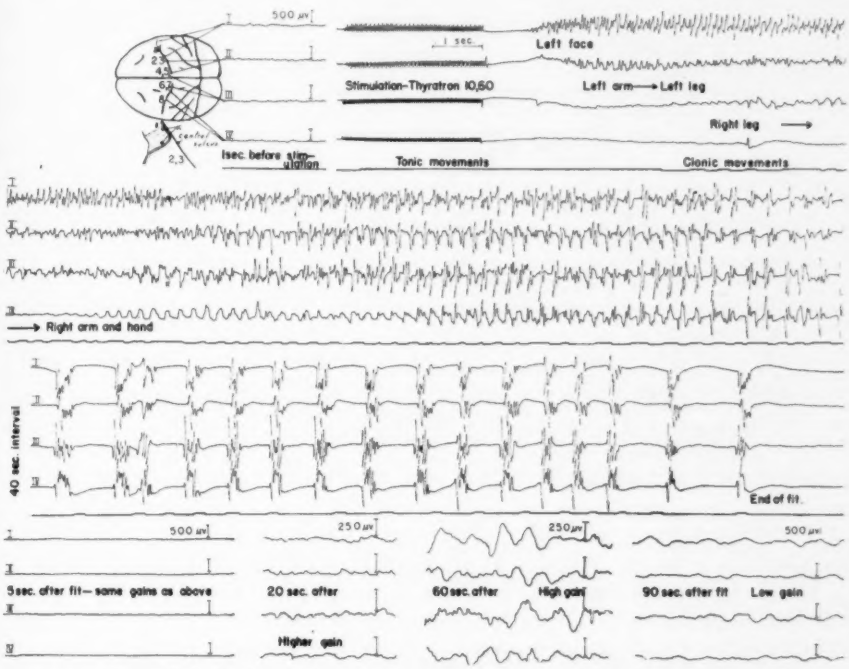

Fig. 1 (P2120, 2D).—This shows the electrogram from four regions of the precentral gyrus of the cortex of a Macaca mulatta monkey before, during and after a convulsion of eighty seconds' duration, initiated by stimulation at *X*, in the face and arm area of the right precentral gyrus. The sequence with which different areas were involved is shown by the electrical changes and also by the onset of clonic movements in various parts of the body, as indicated by the signal record and by the legends directly beneath the electrical record. The sequence of these changes in this record should be compared with that in figures 2, 3 and 4.

A portion of the experiment will be considered in which both the stimulating and the recording electrodes were left entirely unchanged. The recording electrodes were placed one in the leg and one in the arm area of each hemisphere, about 2 mm. anterior to the central sulcus. The stimulating electrode was placed in the lateral part of the right precentral gyrus in the area which gave responses in the left arm and also in the area for the left side of the face and tongue. (In this particular experiment it was not possible to observe the face at all times.)

The first fit resulting from stimulation in this region with an intensity of 10 for three seconds began in the left side of the face and left arm and then spread to involve in turn the left leg, the right leg and the right arm. Observation of the next fit, the electrogram of which is shown in figure 1 (P2120, 2D), showed exactly the same type of spread of the epileptic discharge, as evidenced by the onset of clonic movements. From a study of the electrogram shown in this figure, it is readily seen that the onset of electrical activity of large amplitude corresponds in sequence with that of the jacksonian march.

With this particular arrangement good records of the jacksonian march and of the spread of electrical activity were obtained during eight fits, and each followed the same pattern. This is illustrated again in figure 2 (P2120, 3B), in

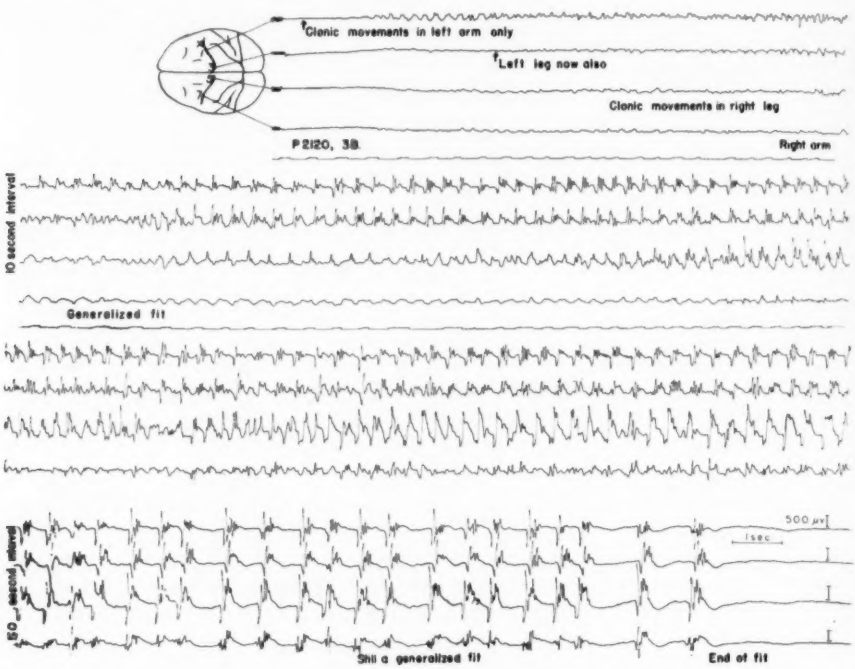

Fig. 2 (P2120, 3B).—Electrogram taken from the same points in the precentral gyrus of the same macaque monkey as in the preceding figure, but with unipolar leads. Stimulation at *X*, in the border between the face and the arm area of the right precentral gyrus, initiated a convulsion of one hundred and twenty seconds' duration, which began in the right arm and marched to other regions, as shown. Although the "jacksonian march" was somewhat slower than that recorded in figure 1, the sequence of involvement of the different limbs was identical. Eight similar fits were recorded, each with the same sequence of spread, before a transcortical section was performed (compare with figure 4).

which *X* indicates the position of the stimulating electrodes and *1, 3, 5* and *7* indicate the positions of the unipolar electrodes, placed as shown on the precentral gyrus of the two sides. Electrode *1,* in the arm area of the right hemisphere, is connected with amplifier I; electrode *3,* in the leg area of the right hemisphere,

is connected with amplifier II; electrode *5*, in the leg area of the left hemisphere, is connected with amplifier III, and electrode *7*, in the arm area of the left hemisphere, is connected with amplifier IV. The signal indicates tonic and clonic movements, and the onset of clonic movements in each limb is indicated by the legend below the tracing from the corresponding area of the motor cortex. It will be noted that the sequence of changes as demonstrated by these two methods is the same, although now changes in the electrogram, now those in clonic movements, precede. These electrodes record from a very small area, only a portion of one arm or one leg area, as the case may be, and clonic movements may precede the appearance of electrical changes due to discharges from some part of a given functional area other than the one from which one happens to be recording.

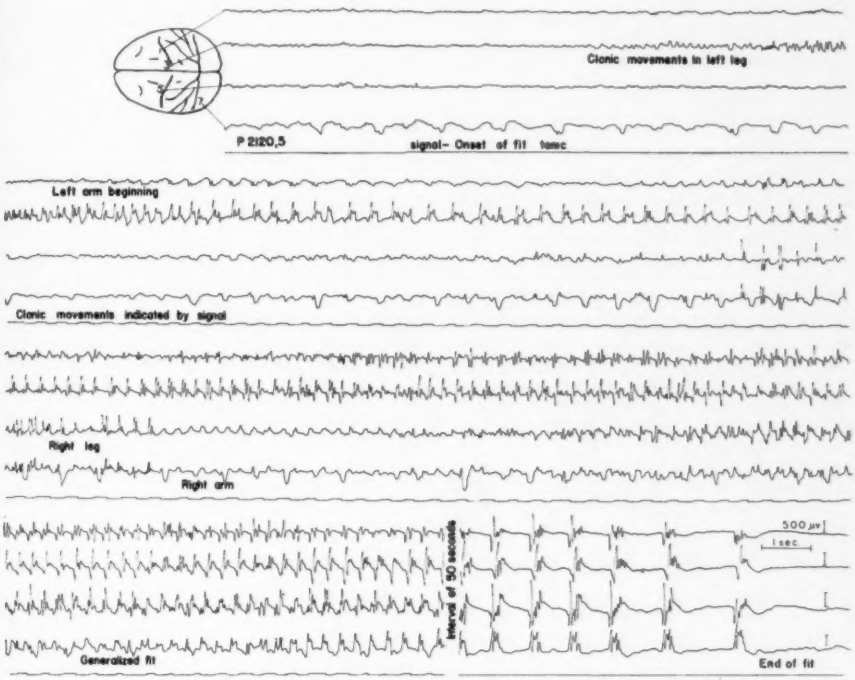

Fig. 3 (P2120, 5).—An electrogram taken directly from the cortex of a Macaca mulatta monkey during a spontaneous fit of one hundred and five seconds' duration. The sequence of the spread and the type of activity are seen to be similar to those of the convulsions initiated by electrical stimulation.

Not infrequently under these experimental conditions, spontaneous fits occur, i. e., without any relation to electrical stimulation of the brain. Such a fit arising in the leg area of the right hemisphere is shown in figure 3 (P2120, 5). It is seen that the general features of the spread of the epileptic discharge are the same; i. e., the entire ipsilateral motor area is involved before the other hemisphere is involved.

After observations were obtained on this monkey during eight fits, a silk suture on a fine curved needle was passed completely under the gray matter of the central sulcus and through the precentral and postcentral gyri at a level just lateral to the area giving ipsilateral responses on cortical stimulation, in the

region of the superior precentral sulcus. The suture was tightly tied so as to produce a clean, sharp section of the gray and white matter of the postcentral and precentral gyri. The whole procedure was carried out without disturbing the stimulating or recording electrodes.

After this section, indicated by *W* in figure 4 (P2120, 7C), the threshold for producing a fit was unaltered, but, as is illustrated in this figure, there was a marked change in the sequence with which cortical areas were involved. The fit started at the point stimulated, the arm area of the right precentral gyrus, but instead of spreading to the adjoining leg area of the same side, as it had before, it now took a circuitous route and spread across (the corpus callosum) to the homologous area in the contralateral hemisphere. This region, even though

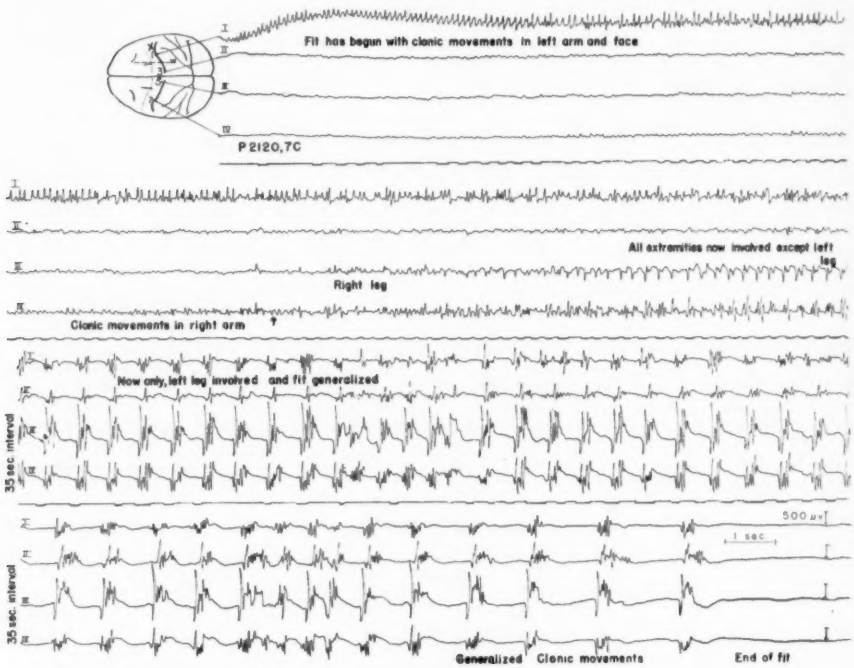

Fig. 4 (P2120, 7C).—Electrogram taken from the precentral gyrus of a Macaca mulatta monkey during a fit of one hundred and thirty seconds' duration, initiated in the right precentral gyrus from the same area (*X*) as the fits records of which are shown in figures 1 and 2. This electrogram, however, was taken two minutes after a transcortical section at right angles to the central sulcus and at the level of the superior precentral sulcus, as indicated by the line *W* in the diagram of the brain. The sequence with which the various portions of the two motor areas were involved by the spreading epileptic discharge, as indicated both by the electrical activity and by the onset of clonic movements, was radically different than that illustrated in figure 2. Neither the recording nor the stimulating electrodes were moved while making the transcortical section. It is evident that direct spread of the epileptic discharge was blocked and its place taken by a circuitous spread. For further details see the text (protocol P2120).

farthest away in actual distance, and in this way the least influenced by possible diffusion of electrical or chemical effects, is presumably closest in a neuroanatomic sense, since the direct pathway across the ipsilateral cortex had been interrupted by the suture section. From the arm area of the left hemisphere the process soon spread to the leg area of the cortex of the left hemisphere. Only after the

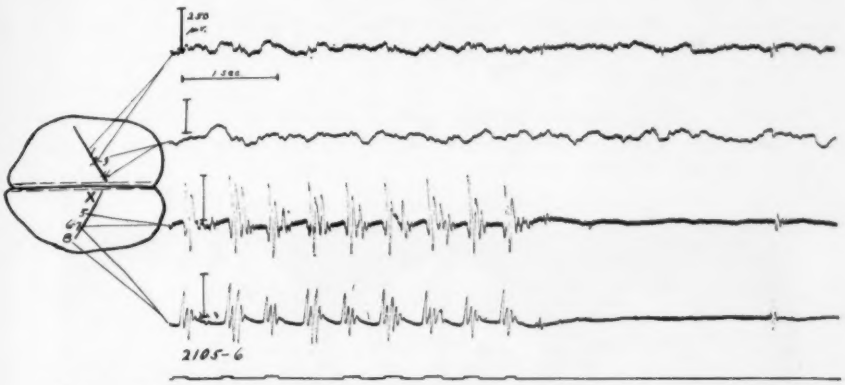

Fig. 5 (P2105, 6).—Electrogram after section of the corpus callosum, showing the end of a fit of one hundred and thirty-five seconds' duration in the right arm and leg produced by stimulation (duration ten seconds, frequency 60 and intensity 6) of the left precentral gyrus at *X*. Compare with figure 6.

Fig. 6 (P2105, 10).—Sample from the corticogram at the end of a fit of fifteen seconds' duration when the stimulating electrode was located on the right precentral gyrus halfway between the electrodes connected with amplifiers I and II, respectively. A study of the electroencephalogram from this animal shows that after complete division of the corpus callosum the epileptiform waves spread all over this hemisphere, but not across the midline to the other hemisphere.

leg area of the left hemisphere began to discharge did the process spread back to the leg area of the right side (ipsilateral area), thus proving that this area was still excitable and showing that the simple section of the cortex and some of the underlying white matter was sufficient to stop a direct spread between contiguous precentral areas. This might be called a circular spread, for if one

considers the two motor areas and the corpus callosum as constituting a circle, the spread was now forced to follow the longest, instead of the shortest, arc of this circle.

However, it must be mentioned that in some cases the fit, after a long delay, appeared to spread around such a simple and rather short section as was used here. In such a case, however, there was a definite delay in the spread, without involvement of the contralateral cortex, so that one can only assume that long, indirect ipsilateral association pathways, rather than short, direct ipsilateral pathways, were involved.

PROTOCOL P2105.—*Macaca mulatta monkey. A chronic preparation; thirteen electrodes over the motor region extradurally; electrocorticogram taken during fits after section of the corpus callosum.*

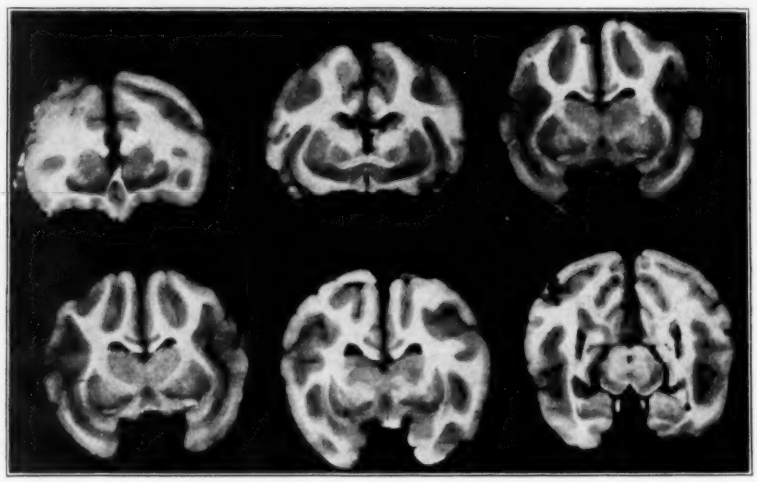

Fig. 7.—Cross sections of the brain of monkey P2105, showing the corpus callosum completely sectioned. Recording electrodes were implanted in the dura at the same time. There appeared to be a minimum of damage to the cortex from either procedure.

In this experiment the corpus callosum was sectioned, using sterile technic, and the animal was allowed to live ten days. At the time of sectioning the corpus callosum thirteen silver electrodes of the usual size, but embedded in two flexible strips of mica and the whole insulated, except at the tips, with bakelite varnish, were placed between the internal and the external layer of the dura and over the region responding to electrical stimulation. The osteoplastic flaps which had been turned down over both cerebral hemispheres were then closed and the electrode leads brought out through the skin.

Seventy-two hours later, when the animal was well recovered from the effects of anesthesia, recording of the electrogram from these implanted electrodes was begun. Stimulation in the leg area of the left hemisphere, as indicated by *X* in figure 5 (P2105, 6), produced electrical change typical of an epileptic discharge limited to the stimulated hemisphere. That the other hemisphere was as susceptible to the epileptic process was shown by subsequent records, such as that in figure 6

(P2105, 10). Previous records for this and other animals had demonstrated that an after-discharge of this severity always spreads to the opposite hemisphere. One can only assume that the division of the corpus callosum had prevented the spread from one hemisphere to the other.

Observation of the extent of the clonic movement is not as simply and directly amenable to analysis. In the convulsion illustrated in figure 5 (P2105, 6), the clonic movements began in the right leg and then spread to the right arm. The same (left) side was, however, also involved in the fit, for there were slow tonic movements on this side the nature of which contrasted sharply with those of the opposite side. These observations are discussed later. That the corpus callosum was completely sectioned with a minimum of trauma to the rest of the brain is shown by the photograph of cross sections of the brain (fig. 7) made when the animal was killed ten days after the operation.

PROTOCOL P2104.—*Macaca mulatta monkey. Cerebellectomy, total section of the corpus callosum, transcortical section, cortical stimulation and electrographic studies.*

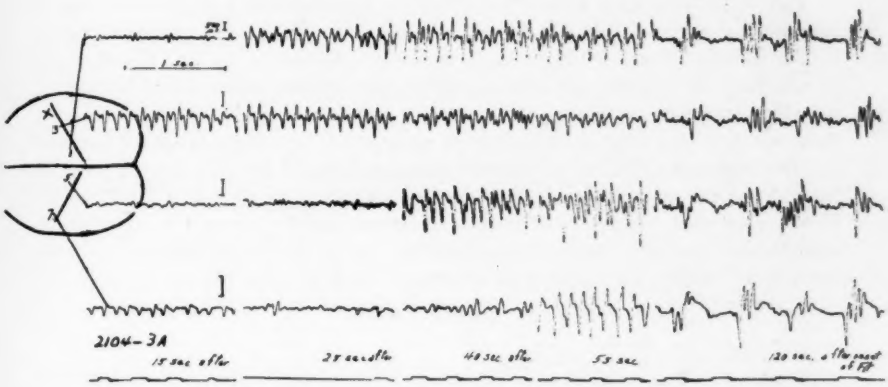

Fig. 8 (P2104, 3A).—An epileptiform fit (after-discharge) of one hundred and forty-five seconds' duration was produced by stimulation at *X*, in the arm area of the right precentral gyrus. Clonus began in the left arm; ten seconds later it appeared in the left leg. Clonic movements did not begin in the right leg until thirty-five seconds after they began in the left arm. The slow march of this fit as evidenced by clonic movements was confirmed by the electrocorticogram.

The upper tracing represents the electrical activity from the leg area, and the second record that from the arm area, of the right precentral gyrus; the third record shows the activity from the leg area, and the fourth that from the arm area, of the left precentral gyrus. It is evident that the sequence of involvement of different portions of the cortex by the electrical changes is similar to the "jacksonian march" of the clonic movements. This figure shows the usual spread of the epileptic discharge in the intact cortex and is to be compared with that after transcortical section (fig. 9).

In this monkey total cerebellectomy was first performed through a suboccipital myoplastic craniotomy opening. After this the animal exhibited marked dyssynergia, ataxia, hypotonia and tremor, with some nystagmus. Two weeks later bilateral craniotomy was performed in the usual manner, exposing the cerebral hemisphere for electrographic studies. The electrical activity during rest was not unusual. Representative of the records obtained during the fits induced by electrical stimulation is that shown in figure 8 (P2104, 3A). The sequence with which different

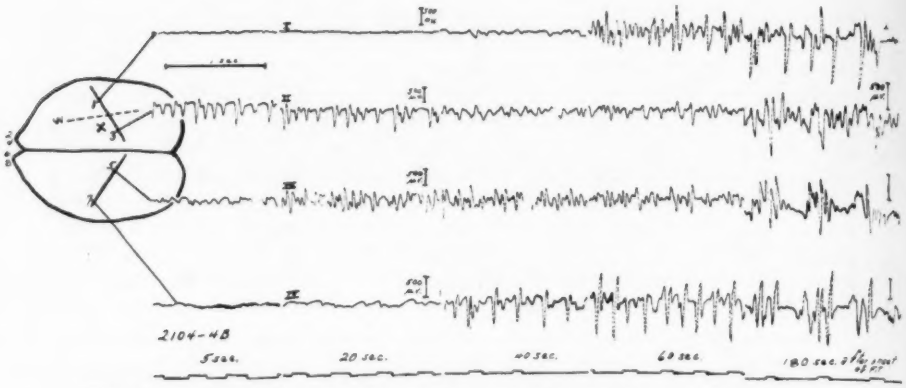

Fig. 9 (P2104, 4B).—These records were taken within five minutes after a transcortical section with silk thread at the plane of *W*, roughly perpendicular to the central sulcus. Stimulation (intensity 5, frequency 60 and duration ten seconds) at *X*, between the longitudinal fissure and the transcortical section of the precentral gyrus, produced a fit beginning locally and spreading until it became generalized, with a total duration of five minutes and five seconds (three hundred and five seconds). The order in which different parts of the cortex were involved by epileptiform activity is made clearer by inspection of the electrocorticogram. It is evident that epileptic activity did not spread directly across the transcortical section (*W*), but had to spread from the region of electrode *3* to electrode *5*, from electrode *5* to electrode *7* and from electrode *7* back to electrode *1*.

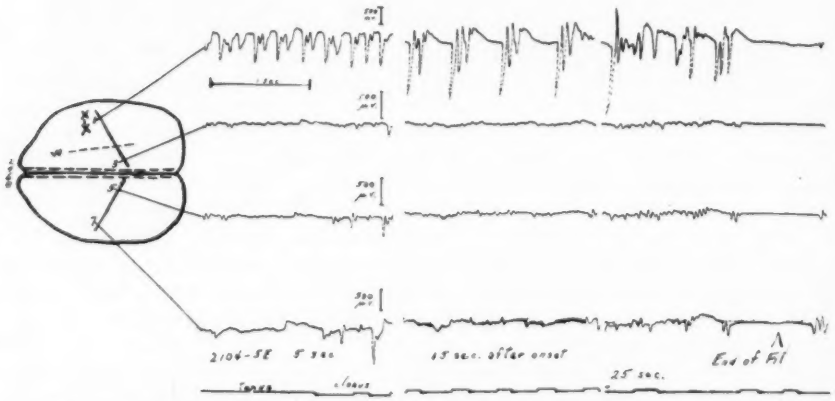

Fig. 10 (P2104, 5E).—Stimulation with a thyratron (intensity 10, frequency 60, duration five seconds) in the arm area of the right precentral gyrus lateral to transcortical section (*W*) and after section of the corpus callosum produced a fit lasting thirty seconds and limited to clonic movements of the left arm. The epileptiform activity shown in the electrocorticogram was limited to a corresponding area of the cortex, i. e., amplifier I, and did not spread as previous similar discharges had done. In other words, both the cortical and the corpus callosal section were effective in interrupting the spread of epileptic activity locally initiated.

functional areas of the cortex were involved by the epileptic activity is typical of that in the intact brain; i. e., the discharge spread to contiguous areas of the ipsilateral cortex before it spread to the other hemisphere.

After repeated observations had established the normal sequence of involvement by the epileptic discharge, a transcortical section (*W*) with a silk suture on a curved round needle was made so as to divide the precentral and postcentral gyri and the gray matter to the depths of the central sulcus. What happened to the sequence of spread is illustrated in figure 9 (P2104, 4B), in which are shown samples of the record during a fit initiated by electrical stimulation at *X*, in the right precentral gyrus medial to the transcortical section. The picture of the spread is particularly clear in the electrogram. The epileptic activity, instead of spreading from the point of its initiation near electrode *3* to the ipsilateral precentral gyrus from which electrode *1* was recording, spread first to the homologous area of the other hemisphere, at electrode *5*, then to the region of electrode *7* and

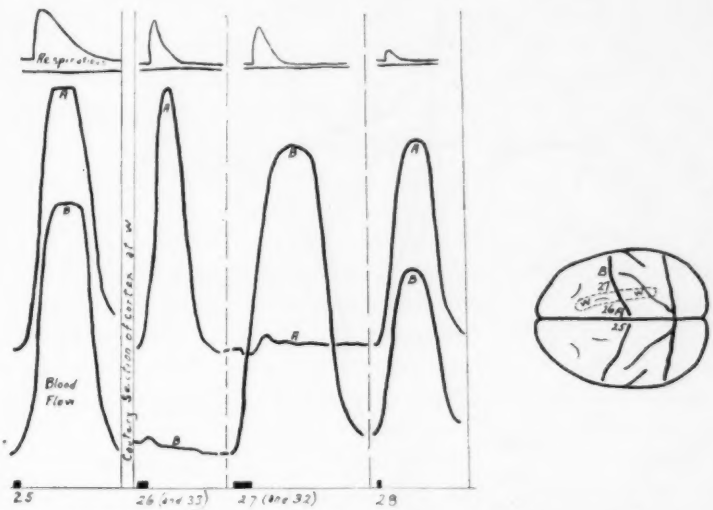

Fig. 11 (P1762).—A tracing of the blood flow recorded from two thermocouples (*A*) and (*B*) before (*25*) and immediately after (*26* and *27*) cortical section at *W*. The fits were produced by stimulation of the precentral gyrus, as indicated on the diagram: at *25*, a generalized fit, of one hundred and two seconds' duration; at *26*, clonic movements of the left and right leg, of forty-five seconds' duration, and at *27*, clonic movements of the left arm, right arm and right leg, of seventy seconds' duration. At *28* epinephrine was injected intravenously.

only later to the contiguous cortex in the region of electrode *1*. The same general type of spread is evident from observation of the clonic movements. It is obvious that the transcortical section at *W* was effective in stopping a direct spread between two contiguous portions of cortex.

Complete section of the corpus callosum was then made. Stimulation near electrode *1* (fig. 10) (and the same was true if stimulation was carried out near electrode *3*) produced a focal epileptic discharge which did not spread beyond the section *W* or across to the other hemisphere. That all portions of both hemispheres were still capable of producing an epileptic discharge themselves or of responding

to activity initiated elsewhere was proved by electrical stimulation, as well as by intravenous injection of metrazol.

PROTOCOL P1762.—*Macaca mulatta. Changes in blood flow in the cerebral cortex recorded by two thermocouples; femoral blood pressure; spread of epileptic discharge, and concomitant focal changes in blood flow blocked by cortical section and by section of the corpus callosum.*

In figure 11 (P1762) are presented tracings from representative records showing the manner in which focal changes in blood flow were employed as an index of epileptic discharge and its spread. The thermocouples, *A* and *B*, in the gray matter of the right precentral gyrus—leg and arm areas, respectively—were used to record the local changes in blood flow. Stimulation at a point (*25*) in the leg area of the left precentral gyrus produced a generalized fit, increase in blood flow being indicated by both thermocouples. A transcortical section, 2 to 3 mm. wide,

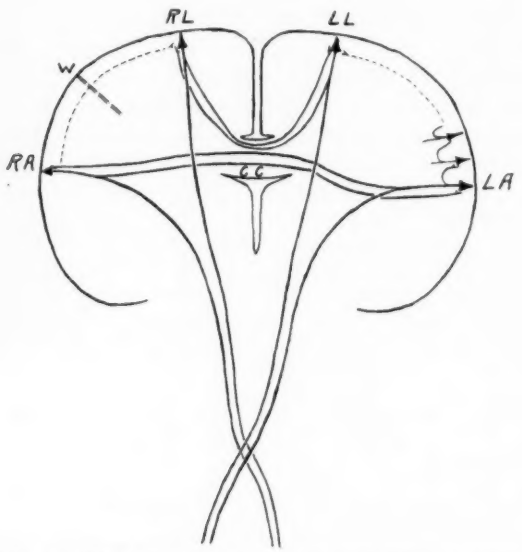

Fig. 12.—This simplified diagram of cortical and callosal fibers is used in discussing the results of experiments on the spread of the epileptic discharge. *RA* indicates the arm area of the right precentral gyrus; *RL*, the leg area of the right precentral gyrus; *LL*, the leg area of the left precentral gyrus; *LA*, the arm area of the left precentral gyrus, and *CC*, the corpus callosum. In the intact animal a fit initiated at *RA* usually spreads in the following manner: *RA*→*RL*→*LL*→*LA*. An ample transcortical section between *RA* and *RL* alters the spread to the following formula: *RA*→*LA*→*LL*→*RL*.

was made through all the gray matter and some of the white, the linear extent being shown in the diagram by *W* (fig. 11). Stimulation at point *25* still produced a generalized fit, with increase of blood flow in both thermocouples. When stimulation was carried out medial to the transcortical section, at *26*, the change in blood flow was limited to thermocouple *A*. With stimulation at *27*, lateral to section *W*, the increase in blood flow was limited to thermocouple *B* if the fit did not spread. When, however, the fit became generalized a delayed change in blood

flow appeared in the thermocouple on the other side of the transcortical section as the discharge spread to the corresponding area of cortex.

Many variations in this setup, using thermocouples in different areas and initiating a fit by electrical stimulation, have confirmed the various features of the spread, which have been illustrated more clearly by means of the electrographic records. The femoral blood pressure was recorded in all instances, and only the records were accepted in which the changes in blood flow appeared to be independent of alterations in blood pressure.

COMMENT

The great similarity between the convulsions produced by electrical stimulation of the cortex and certain forms of clinical epilepsy is striking to any one who has observed them. The fact that the electroencephalographic picture of these experimentally produced fits, as well as the changes in blood flow, is similar to that in grand mal seizures indicates that the two processes are closely allied and that one can, with due circumspection, consider them as interchangeable.

That the electrographic changes during a fit are not recording artefacts due to the movement of the electrodes is shown by several facts. The characteristic epileptic waves of electrical potential appear first in the zone of stimulation, and at this time may remain localized to the region of one electrode for several seconds before spreading to involve others. If movement of the head were causing these waves, one would expect all the electrodes to be affected equally, in a manner similar to the disturbance which can readily be seen when movement of the head does take place. Moreover, the type of disturbance caused by movement or by local muscle potentials is easily distinguishable from the wave characteristic of epilepsy. Another good piece of evidence is furnished by inspection of the record of an animal, such as P2105 (figs. 5 and 6), in which the corpus callosum has been cut. The strictly unilateral, but violent, clonic movements are always in the extremities on the side opposite that in which the stormy changes of electrical potential are occurring, while the ipsilateral cerebral cortex shows a remarkable calm. Artefacts due to movement could not account for such a distribution.

That the electrographic changes in these fits are not artefacts produced by the stimulating current is evident, for the source of the stimulating current (60 cycle) is entirely disconnected from the animal before recording is begun. The changes which have been studied occur and develop over periods ranging from one second to five minutes after cessation of electrical stimulation.

Role of the Corpus Callosum in Spread of the Epileptic Discharge.—My observations on the spread of the epileptic discharge from one cerebral hemisphere to the other indicate that this spread occurs largely or entirely via the corpus callosum. These findings were possible only by use of the electroencephalogram and the changes in blood flow as

indications of local neuronal activity, and because of recent advances in knowledge concerning representation of the extremities in the ipsilateral cerebral hemisphere.

It is clear from my experiments that section of the corpus callosum alters not only the spread of the electrical potential and changes in blood flow concomitant with the epileptic discharge, but also the character of the movements during a fit initiated by electrical stimulation of a restricted area of one hemisphere. Instead of producing a tonic phase followed by generalized clonic movements, as occurs before such section, there are usually generalized tonic movements followed by clonic movements limited to the contralateral half of the body. Occasionally there are slight clonic movements in the ipsilateral half of the trunk and in the proximal muscles of the ipsilateral limbs after section of the corpus callosum. There are not, however, clonic movements in the distal portions of the ipsilateral extremities, as there are in the contralateral extremities, and it is difficult to discern whether or not these proximal limb movements are entirely secondary to the violent clonic contraction of the other side. Often, if the muscles are carefully palpated it is clear that the movements are entirely passive and secondary. Usually there is only a slow tonic extension of the ipsilateral extremities, while the contralateral extremities exhibit the typical clonic contractions of the after-discharge. Electromyograms from the ipsilateral and contralateral extremities illustrate this distinct difference.

Excision of the ipsilateral area as localized by electrical stimulation was carried out after section of the corpus callosum. The ipsilateral movements were then abolished when stimulation resulting in a fit was carried out on the side of excision, although the contralateral clonic movements persisted in undiminished form. A fit arising from the other hemisphere showed the usual tonic ipsilateral movements.

Clinically, these slow tonic movements may be frequently observed in cases of focal epilepsy, beginning with turning of the head and eyes or with clonic movements of the upper extremities. These appear to be directly comparable with the movements initiated from the ipsilateral cerebral cortex in monkeys. Bucy and Fulton [24] demonstrated that ipsilateral responses of the extremities can be obtained by stimulation in a restricted region about the superior precentral sulcus in the monkey. The excitable area lies principally in area 6 of Brodmann, but it may also extend into the anterior limit of area 4. These ipsilateral responses are independent of the contralateral responses with which they are associated and are mediated by a pathway which is entirely ipsilateral. Wyss [25] has recently confirmed these observations by using

24. Bucy, P. C., and Fulton, J. F.: Ipsilateral Representation in the Motor and Premotor Cortex of Monkeys, Brain **56**:318-342, 1933.

25. Wyss, O. A. M.: On an Ipsilateral Motor Effect from Cortical Stimulation in the Macaque Monkey, J. Neurophysiol. **1**:125-126, 1938.

stimuli of optimal duration. Ipsilateral responses have been observed in man after cortical stimulation by Penfield (personal communication), as well as by others mentioned by Bucy and Fulton.

Failure to appreciate the importance of such an ipsilateral response accounts for the erroneous conclusion reached by some earlier workers (e. g., Karplus,[5] Spiegel and Falkiewicz [6] and Spiegel [7]) that the corpus callosum plays no part in the spread of the epileptic discharge from one hemisphere to the other. It is now evident that an epileptic discharge limited to one hemisphere by section of the corpus callosum may still produce movement in all four extremities by initiating a discharge from cells governing ipsilateral as well as contralateral movements.

More graphic evidence of the role of the corpus callosum in the spread of the epileptic discharge has been furnished by the electroencephalogram. As can be seen by inspection of any of the protocols for monkeys with complete section of the corpus callosum, the typical epileptic disturbances in potential did not spread to the hemisphere opposite the one in which they were initiated by electrical stimulation. Before section of the corpus callosum they invariably did so, if a good after-discharge was produced which involved all the motor area on the side stimulated. That this was not due to loss of excitability of the other hemisphere has been repeatedly demonstrated.

An apparent exception must be discussed. In 1 monkey, which was having rather frequent spontaneous seizures, epileptic activity appeared in both hemispheres after restricted stimulation of the one motor region, even though the corpus callosum had been sectioned. The time relation between the onset of epileptic discharge on the two sides was quite different from that in the other experiments. Since this monkey was having frequent spontaneous fits, it appears safe to regard this response as merely a spontaneous fit arising coincidentally in the other hemisphere. Although these experiments indicate that the corpus callosum plays a major role in the spread from one hemisphere to the other, I have not produced positive evidence that some other pathway, such as that through the pons suggested by Spiegel and Falkiewicz,[6] may not play a subsidiary role. Studies of the changes in blood flow lead me to the same conclusion regarding the role of the corpus callosum as to studies of the electrogram.

Either strychnine applied locally [18] or electrical stimulation under conditions of anesthesia preventing a general epileptic discharge should reveal details of anatomic connections between the two hemispheres in higher mammals which have so far defied histologic methods of investigation. Curtis and Bard [26] have recently studied the intercortical connections of the corpus callosum as indicated by evoked potentials.

26. Curtis, H. J., and Bard, P.: Intercortical Connections of the Corpus Callosum as Indicated by Evoked Potentials, Proc. Am. Physiol. Soc., 1939, p. 57.

A priori, if the spread takes place over neuronal pathways, one would expect to find that the corpus callosum furnishes a pathway for the spread of the epileptic discharge from one hemisphere to the other, as has been shown in this paper. If, on the other hand, the corpus callosum plays no part in the spread it would be presumptive evidence that the spread occurs in some manner other than by neuronal pathways —either by a vascular mechanism, such as was suggested by Jackson, or by the diffusion of some humoral agent, alpha substance (Penfield [27]), which at the same time is responsible for the change in blood flow.

Since it has been proved by my experiments that the corpus callosum does play a major role in the spread of the epileptic discharge, one has strong evidence that the spread takes place over neuronal pathways. This is represented schematically in figure 12. The callosal fibers arise as collaterals of large pyramidal cells, as well as from processes of smaller cortical cells (Ramón y Cajal [28]). The latter are not represented in this schematic diagram, nor are the ipsilateral centers and pathways.

Partial division of the corpus callosum, even of all the fibers responding to electrical stimulation (Mott and Schaeffer [29]), does not abolish the spread of epileptic discharge from one hemisphere to the other, although it may cause delay.

Attempts at localization of epileptic foci in man show that "epileptiform waves" are often picked up from homologous regions of the two cerebral hemispheres, much to the confusion of facile electroencephalographic localization. Golla, Graham and Walter,[30] in an electroencephalographic study of epilepsy, pointed out the frequent occurrence of "mirror" foci. The occurrence of "mirror" foci was also noted by Gazzano [18] in the course of a study of reflex epilepsy. After application of strychnine to a point in the cortex of one hemisphere, a discharge of spikes also developed in the opposite hemisphere. As with the afterdischarge produced by electrical stimulation, this strychnine discharge in the opposite hemisphere could be abolished by section of the corpus callosum.

Of 5 patients with agenesis of the corpus callosum reported on by Hyndman and Penfield,[31] 4 were observed because of epilepsy. In 2 cases the fits were of a petit mal type, and in 2 there were clonic move-

27. Penfield, W.: The Circulation of the Epileptic Brain, A. Research Nerv. & Ment. Dis., Proc. (1937) **18**:605-637, 1938.

28. Ramón y Cajal, S.: Histologie du système nerveux de l'homme et des vertébrés, translated by L. Azoulay, Paris, Norbert Maloine, 1911, vol. 2.

29. Mott, F. W., and Schaeffer, E. A.: On Movements Resulting from Faradic Excitation of the Corpus Callosum in Monkeys, Brain **13**:174-177, 1890.

30. Golla, F.; Graham, S., and Walter, W. G.: The Electroencephalogram in Epilepsy, J. Ment. Sc. **83**:137-155, 1937.

31. Hyndman, O. R., and Penfield, W.: Agenesis of the Corpus Callosum: Its Recognition by Ventriculography, Arch. Neurol. & Psychiat. **37**:1251-1270 (June) 1937.

ments on the right side without positive evidence of spread to the opposite side. Although generalized seizures are reported as occurring in patients with tumors of the corpus callosum (Voris and Adson [32]), no adequate or detailed description of the attacks is available, and I cannot but wonder, in the light of 2 cases I have personally observed, whether a truly generalized fit occurs in the presence of complete agenesis or surgical section of the corpus callosum in man.

Spread of the Epileptic Discharge Across the Cerebral Cortex.—The spread of the epileptic discharge induced by restricted electrical stimulation of a point in the motor region of the cortex is altered by a transcortical section, of sufficient extent, at right angles to the central sulcus. Under the conditions of my experiments the monkeys are highly susceptible to the production of convulsions by electrical stimulation of the cortex. A momentary application of the stimulating current to a point in the motor area produces a focal motor response which continues after withdrawal of the stimulus. These changes spread relatively slowly to contiguous areas of the cortex, and only later to the cortex of the contralateral hemisphere. This march can be followed by any of the three indexes of epileptic activity which have been used. A single transcortical section of proper extent produces an alteration in the sequence of this march. The most characteristic of these is the circuitous spread, which has been illustrated in figures 1 to 4 and figures 8 and 9. This may be summarized by reference to the diagram in figure 12. If an epileptic discharge is initiated in the arm area (*R A*) of the right hemisphere, it spreads in the intact cortex to the contiguous leg area (*R L*), and then to the contralateral arm and leg areas, represented by *L A* and *L L*, respectively. If, however, a transcortical section is made so as to interrupt the cortex between the arm and the leg area, of the right side at *W* (fig. 12), the march of the epileptic process assumes a different configuration. Now a discharge initiated in the same place, the arm area of the right hemisphere (*R A*), does not pass directly to the contiguous portions of the ipsilateral cortex (*R L*), but spreads to the contralateral arm area (*L A*), back to the leg area of the left side (*L L*) and, finally, to the leg area of the right hemisphere (*R A*). Two such transcortical sections should furnish information concerning the heterotopic and homotopic distribution of the callosal fibers. That the callosal fibers are involved in this spread cannot be doubted from the experiments previously presented. It has been proved directly, however, by division of the corpus callosum after such a transcortical section.

32. Voris, H. C., and Adson, A. W.: Tumors of the Corpus Callosum: Pathologic and Clinical Study, Arch. Neurol. & Psychiat. **34**:965-972 (Nov.) 1935.

The specific nature of the transcortical sections producing this effect must be more fully discussed, especially as to their relation to the anatomic substrata involved and to their surgical nature.

To test various theories of the spread of the epileptic discharge, the effect of different types of transcortical section was investigated. A lesion of appreciable width, such as that produced by excision or coagulation of a strip several millimeters wide, may produce a different situation than the simple severance of nerve connections produced by drawing together a simple silk suture passed through the cortex on a curved needle. There would still be direct coaptation of viable neural tissues after a lesion produced by the latter method, provided care was taken to avoid hemorrhage. The continuing direct coaptation of the surfaces of neural tissue would presumably not interfere with the diffusion of an alpha substance,[27] if such were responsible to any extent for the spread or initiation of the epileptic discharge. The fact that such a simple transcortical section was just as effective in altering the spread as a wide lesion may be regarded as evidence against such an alpha substance playing a major role in the spread of the epileptic discharge and in favor of the view that the spread is solely via neuronal pathways. Such a conclusion, of course, does not deny the local effect of an alpha substance on neuronal discharge or in the causation of the associated changes in blood flow.

Although the effectiveness of a section in stopping the spread of the epileptic discharge across the cortex did not depend on such factors as width, it seemed to depend intimately on the completeness with which the precentral and postcentral gyri and the depths of the central sulcus were severed. The anteroposterior extent of the section also appeared to be important. If it did not extend well into the precentral and postcentral gyri it was difficult to demonstrate any effect on the spread. Presumably, even though the direct pathway was interrupted, it could by other association pathways spread quickly around the end of this transcortical section with little delay, and so could not be demonstrated by the methods I have used. If the anteroposterior extent of the section is sufficient, the resistance to this form of spread becomes so great that the spread is radically altered in its sequence, as has been illustrated and reported in the protocols. Isolation of portions of the cortex is being carried out, in order to study this problem more exactly.

These transcortical sections, to be effective in stopping the spread, appear of necessity to sever connections as deep as the inner surface of the gray matter at the depths of the central sulcus. Whether intracortical fibers account for the spread or whether the spread takes place by short association fibers passing through the white matter immediately subgriseal cannot as yet be definitely stated, and these problems are being investigated further. An intracortical pathway for the spread cannot be ruled out, but it appears that short subcortical association

fibers are mainly concerned. Evidence in favor of this view is furnished by the work of Dusser de Barenne, McCulloch and their associates.[10] They found no change in the distribution of spikes induced by local strychninization of the sensorimotor cortex after thermocoagulation of a narrow circular strip of cortex over the entire thickness of that cortex around the strychninized locus, or by deep undercutting of the whole sensorimotor cortex. They concluded that axons from the area strychninized run through the white matter of the pallium to the other areas in which strychnine spikes appear, but that, as they pointed out, these findings do not preclude the operation of intracortical, i. e., intragriseal, axons as well.

The types of transcortical sections which have been demonstrated in my experiments to limit the spread of the epileptic discharge do not greatly injure projection fibers to and from the basal ganglia. Hence it seems probable that these pathways are not of such primary importance in the spread of the discharge as are the corticocortical pathways. This does not deny to them a subsidiary part in the spread and manifestations of the epileptic discharge.

Is the entire cerebral cortex involved during a generalized fit? As judged by the electrical activity, it is. The changes in blood flow, however, often appear to be limited to the motor and sensory areas.[11] It is often difficult to be certain of these changes during a generalized fit because of the marked changes in blood pressure. In some experiments I have observed a general increase in cortical blood flow in both the frontal and the occipital pole, and at other times a decrease. The latter fact, a relative decrease of blood flow in nonactive areas, may explain the histopathologic evidences of anemia reported by Spielmeyer [33] in the hippocampus and the cerebellum of brains of epileptic persons.

SUMMARY AND CONCLUSIONS

The spread of the epileptic after-discharge induced in monkeys by electrical stimulation of the cerebral cortex has been studied, using several indexes of epileptic activity. These indexes are, first, the spread of clonic movements; second, the local changes in the electrical activity of the cerebral cortex, and, third, the local changes of blood flow in the cerebral cortex during epileptic activity. These changes, which in themselves cast light on the nature of the epileptic discharge, cast additional light on the nature of the epileptic discharge by helping to reveal the manner in which the epileptic discharge spreads. Two types of procedures altering the spread of this discharge have been carried out, namely, section of the corpus callosum and transcortical section at right angles to the central sulcus of Rolando.

33. Spielmeyer, W.: Die Pathogenese des epileptischen Krampfes, Ztschr. f. d. ges. Neurol. u. Psychiat. **109**:501-520, 1927; The Anatomic Substratum of the Convulsive State, Arch. Neurol. & Psychiat. **23**:869-875 (May) 1930.

This study has concerned mainly the motor regions, so as to correlate the motor manifestations of the fit with the other concomitant phenomena of the epileptic discharge. Some observations have been made on other areas of the cerebral cortex. The following conclusions have been reached:

1. The after-discharge induced by electrical stimulation of the cortex is a faithful experimental counterpart of clinical types of epilepsy. Various motor variants have been observed which appear to be identical in their characteristics with those seen in certain clinical forms of epilepsy. The changes in blood flow in these animals during fits are the same as those seen in man during epileptic fits. The changes in electrical potential during and after epileptiform fits are the same in monkeys as they are in man during epileptic seizures.

2. A constant type of fit is easily reproducible in monkeys by electrical stimulation of the cortex. A study of the various factors which influence it renders the mechanism of these epileptiform fits accessible to experimental analysis.

3. The corpus callosum plays a definite role in the spread of the epileptic discharge from one hemisphere to the other, and this is demonstrable by all the indexes of epileptic discharge, although it is best recorded and illustrated graphically by the electrical activity.

4. Epileptic discharge from one hemisphere, if widespread over that cortex and prevented from spreading to the other hemisphere by section of the corpus callosum, gives rise to contralateral clonic movements and ipsilateral slow tonic movements, the latter being due, at least in part, to epileptic discharge from an area in the premotor region governing ipsilateral movements.

5. Epileptic discharge of the neurons of the ipsilateral areas of the cerebral cortex gives rise to a large part of the tonic element of the convulsion.

6. Transcortical section at right angles to the central sulcus, if it is of sufficient extent in a sagittal direction and of sufficient depth, alters the pathway for the spread of the epileptic discharge. This appears to be due to interruption of certain corticocortical association pathways. A significant characteristic circuitous pathway involving the corpus callosum and contralateral motor cortex is then evident in the spread of the epileptic discharge.

7. With the cerebral cortex intact, subcortical centers play a secondary role in the spread of the epileptic discharge.

8. The spread of the epileptic discharge takes place by neuronal pathways.

EXPERIMENTAL EVIDENCE OF ANTICONVULSANT PROPERTIES OF SODIUM DIPHENYL HYDANTOINATE (DILANTIN SODIUM N. N. R.)

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Putnam and Merritt,[1] in a study of various anticonvulsant drugs, concluded that sodium diphenyl hydantoinate is a highly effective anticonvulsant which compares favorably with phenobarbital and is far superior to bromides. They administered various drugs having possibilities as anticonvulsant agents and then applied electrical stimulation of sufficient strength to produce convulsions. The work of Merritt, Putnam and Schwab [1b] was done exclusively on animals, the cat being used as the experimental test animal. It was found that animals have a characteristic threshold, with variations of less than 10 per cent for any one day. Merritt and Putnam [1c] expanded their study to the use of sodium diphenyl hydantoinate as a drug for the treatment of epilepsy and found that 58 per cent of their patients were completely relieved from attacks for a considerable period.

The authors felt that additional evidence of raising of the convulsive threshold in human subjects by the administration of sodium diphenyl hydantoinate was desirable. An opportunity was afforded us by another study to demonstrate in patients that, aside from the clinical evidence afforded by the drug in diminishing the frequency of seizures, sodium diphenyl hydantoinate also had a definite anticonvulsant action when a pharmacologic agent with convulsive properties was used after sodium diphenyl hydantoinate had been previously administered.

From the Chicago State Hospital, Edward F. Dombrowski, M.D., Managing Officer.

1. (*a*) Putnam, T. J., and Merritt, H. H.: Experimental Determination of the Anticonvulsant Properties of Some Phenyl Derivatives, Science **85**:525 (May 28) 1937. (*b*) Merritt, H. H.; Putnam, T. J., and Schwab, D. H.: A New Series of Anticonvulsant Drugs Tested by Experiments on Animals, Arch. Neurol. & Psychiat. **39**:1003 (May) 1938. (*c*) Merritt, H. H., and Putnam, T. J.: Sodium Diphenyl Hydantoinate in the Treatment of Convulsive Disorders, J. A. M. A. **111**:1068 (Sept. 17) 1938.

MATERIAL AND METHOD

Nineteen female patients in whose cases a diagnosis of epilepsy had been made by the medical staff of the Chicago State Hospital, and who were the subjects of an experimental study undertaken by Gellhorn, of the department of physiology of the University of Illinois, were given a subcutaneous injection of 5 cc. of a 10 per cent solution of metrazol per hundred pounds (about 45.5 Kg.) of body weight. The metrazol was injected in the inner aspect of the thigh and distributed so as to permit ready absorption. The patients were observed for two hours after the injection. Although other studies were made on these patients, in this paper we are reporting only on a qualitative determination of the effectiveness of sodium diphenyl hydantoinate (dilantin sodium N. N. R.) as an anticonvulsant drug.

RESULTS

Ten patients, or 52.68 per cent, had grand mal seizures after the injection of metrazol. Four patients presented symptoms which could be classified as variant convulsive tendencies. One showed clonic movements, which began shortly after the injection and persisted for some time. Three had psychomotor equivalents, which lasted for several minutes. The precentage of patients who presented epileptic aberrant reactions was 21.05. When this is added to the percentage of patients who had a grand mal seizure, the total percentage of patients with definite convulsive tendencies is 73.73. In the cases of the 10 patients who had grand mal seizures, the length of time between administration of the metrazol and the seizures is recorded in the accompanying tabulation:

No. of Patients	Period
6, or 60 per cent	0 to ½ hour
3, or 30 per cent	½ to ¾ hour
1, or 10 per cent	¾ to 1 and ½ hour

Of the patients who had seizures after injection of metrazol, 4 had more than one grand mal attack, 2 having three and 2 two seizures. None of the patients who had more than one seizure had received sodium diphenyl hydantoinate.

Fifteen patients, all except 4 of whom had undergone the previous test, were given sodium diphenyl hydantoinate (dilantin sodium) in sufficient doses to reduce the frequency of seizures without causing any severe toxic symptoms. After sodium diphenyl hydantoinate had been given for from one to several months, metrazol was administered in the dose of 5 cc. of a 10 per cent solution per hundred pounds of body weight. Of the 14 patients treated, 1, or 7.14 per cent, had a grand mal seizure. Three patients had typical petit mal seizures, and 1 had a period of confused behavior. If all the convulsive substitutes are included, the total percentage of patients with convulsive tendencies is 35.71.

The following tabulation presents the figures more definitely.

	Metrazol Reactions Before Sodium Diphenyl Hydantoinate Was Given	*Metrazol Reactions After Sodium Diphenyl Hydantoinate Was Given*
	Total No. of patients: 19	Total No. of patients: 15
Percentage of patients with grand mal.....	52.68	7.14
Percentage of patients with petit mal.....	21.05	28.57
Percentage of patients with no reaction.....	26.27	64.29
Total reaction.....	73.73	35.71

SUMMARY AND CONCLUSION

Sodium diphenyl hydantoinate has recently been introduced by Putnam and Merritt as a drug with anticonvulsant action greater than that of bromides and equal to that of phenobarbital.

In a group of epileptic patients given metrazol subcutaneously the number of seizures produced was in excess of 52.68 per cent.

When sodium diphenyl hydantoinate (dilantin sodium N. N. R.) was given for one month or longer previous to the administration of metrazol the number of grand mal seizures fell to 7.14 per cent.

Putnam and Merritt expressed the belief that sodium diphenyl hydantoinate is more effective against grand mal than against petit mal seizures or epileptic equivalents. The fact that petit mal seizures occurred in 21.05 per cent of patients who had not been given sodium diphenyl hydantoinate and in 28.57 per cent of patients who had received the drug is interesting.

Sodium diphenyl hydantoinate has anticonvulsant properties which are demonstrable by administration of metrazol subcutaneously in a group of epileptic patients before and after sodium diphenyl hydantoinate is given.

HEAT-REGULATORY MECHANISMS IN NORMAL AND IN SCHIZOPHRENIC SUBJECTS

UNDER BASAL CONDITIONS AND AFTER THE ADMINISTRATION OF DINITROPHENOL

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Numerous researches of the investigative and therapeutic type have indicated that there exists in schizophrenia some abnormality of the autonomic nervous system, particularly of the sympathetic division. The conclusions, however, have not been definitive, and it was with the hope of throwing further light on this aspect of the problem that the present study was undertaken. It concerns an attempt to estimate this dysfunction quantitatively by studying it from the point of view of heat regulation. Since the vasomotor activity of the organism is intimately related to its thermal equilibrium and since this status can be accurately measured, such information as may be derived from the study may be expected to shed light on certain aspects of autonomic reactivity.

METHOD AND MATERIAL

In this research studies were carried on under quiet resting ("basal") conditions and also in a "stress" situation in which the organism was forced to adapt to a new thermal situation. For the latter, dinitrophenol was used because of its rapidity of action and its generalized metabolic effect. Heat production was determined by means of the rate of oxygen consumption, and heat dissipation was evaluated by measurements of skin temperature and the evaporation of perspiration through the skin and lungs.

The subjects utilized in this study included 20 normal male subjects and 20 male schizophrenic subjects free from organic disease. The patients and normal subjects were matched for height and weight and were tested in pairs. Each normal control lived at the hospital for the duration of the study in a room adjacent to that of the patient, so that the environmental situation was similar for each group. The study was carried on throughout the winter and spring months, so that seasonal variation was balanced.

The investigation was carried out in an air-conditioned laboratory in which environmental factors could be satisfactorily controlled. Measurements of skin and rectal temperatures were made by iron-constantin thermocouples. The oxygen consumption rate was measured by means of a Benedict-Roth apparatus.

The rate of evaporation of insensible perspiration was determined by means of a Sauter balance, which when loaded was accurate within 0.15 Gm. In

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order that a graphic record might be obtained, the balance arm was extended by means of a rod. A writing point suspended from the end of this rod traced on a kymograph the loss of weight of the subject. A time record was obtained simultaneously. As the scale was extremely sensitive to the slightest movement of the subject, an electromagnetic damping device [1] was constructed to minimize the extent and duration of such oscillations, thus allowing the securing of a fairly smooth graph.

All studies were made under the same environmental conditions. A neutral zone of air temperature [2] was chosen at which heat loss and heat production would be equal, so that metabolic changes due to environmental factors would be kept within a minimum. The air temperature was maintained at 30 ± 0.3 C. (86 ± 0.5 F.). The relative humidity was kept at an average level of 20 ± 2 per cent. The movement of air in the room was slow, the average rate of air flow being 5 ± 1 feet (152 ± 30 cm.) per minute. The variations in the environmental conditions were thus in all probability too small to have any physiologic significance.

The investigation covered two separate days. On the first day the measurements were made under strictly basal conditions. This is called the "basal" day, and the values serve as a base line for the other determinations. On another day, seventy-two hours later, the subjects were given 300 mg. of dinitrophenol by mouth, one hour before entry to the laboratory.

The procedure followed on the experimental days was as follows: The subjects were kept in bed fasting until 9 a. m., when they put on bathrobes and slippers and went downstairs to the laboratory. There they immediately disrobed and lay down on coarsely woven cane beds without covering. Thirty minutes later and twice subsequently at one hour intervals, measurements were made of the skin and rectal temperatures, the oxygen consumption rate and the rate of loss of insensible perspiration. Skin temperatures were measured on the forehead and nine other points on the right anterior surface of the body on the chest, the abdomen, the upper and lower portions of the arm, the thenar eminence, the tip of the middle finger, the upper and lower portions of the leg and the foot. The bilateral symmetry of skin temperatures in subjects without circulatory disorder is so great that a study of one side of the body is sufficient.[3] Single determinations were made of the oxygen consumption rate at a given period. The rate of evaporation of insensible perspiration was measured over an interval of twenty to thirty minutes.

From table 1 it will be seen that the height and weight of the two groups were so similar as to indicate that their metabolic status was practically identical. The patients were on an average ten years older than the normal subjects, but the age distribution in both groups was such as to exclude both adolescence and senescence, with a consequent minimizing of physiologic variation. The period of hospitalization of the patients averaged eight and three-tenths years, with a range of from one to twenty-three years; 70 per cent had been in the institution

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more than five years. One may thus conclude that the patients were in a chronic stage of the psychosis. Thus, any conclusions that may be drawn from the investigations are simplified, since other studies have indicated the existence of differences between patients in the acute and those in the chronic stage of the psychosis.

RESULTS

The experimental data will be presented in two sections: first, those derived on the "basal" days and, second, those obtained after the administration of dinitrophenol. Thus there will be afforded an opportunity of comparing schizophrenic patients with normal subjects under conditions in which the body does a minimal amount of work and in which a metabolic stress situation has been imposed on it.

The means of the various functions studied on the two days are shown in table 2. The skin temperatures of the forehead, trunk and upper portions of the extremities have not been included in the table, since their levels showed no

TABLE 1.—*Statistics on Weight, Height and Age of 20 Schizophrenic Patients and 20 Normal Control Subjects and on the Period of Hospitalization of the Patients*

	Normal Control Subjects				Patients			
	Minimal	Maximal	Mean	Standard Deviation	Minimal	Maximal	Mean	Standard Deviation
Weight, Kg.	46.4	75.8	62.8	8.0	44.5	75.7	62.6	8.3
Height, cm.	161.6	187.4	172.6	7.0	161.0	184.3	171.3	6.1
Age	18	36	23 3	4.2	23	49	33.5	7.0
Period in hospital, yr.	..	..	..	...	1	23	8.3	5.9

change either on the "basal" or on the dinitrophenol days. Discussion of the skin temperature will consequently be confined to that of distal points on the extremities.

On the "basal" day, exposure to the environmental conditions resulted in a rise in skin temperature, which was more marked in case of the normal subjects than of the patients. In the former group the temperature increased 0.6 C. (1.1 F.) on the thenar eminence and 1.2 C. (2.16 F.) on the finger and showed no change on the foot. For the patients the corresponding changes were an increase of 0.4 C. (0.7 F.) (which was transient) on the thenar eminence and 0.2 C. (0.36 F.) on the finger and a fall of 0.4 C. (0.7 F.) on the foot.

In the rectal temperature, a slight and essentially equal fall was found in the patients and the normal subjects. The decline in rectal temperature is probably due to the relaxation attendant on the maintenance of the recumbent posture and is found at all environmental temperatures except those sufficiently high to inhibit heat loss from the organism.

With respect to the oxygen consumption rate, the normal subjects had an initial reading of 93 per cent of prediction. During the next two hours this level rose to 100 per cent, an elevation which, in view of the neutrality of the environment, was probably due to the restlessness of the subjects. For the patients, on the other hand, the initial rate was 89 per cent, a value slightly lower than that of the normal subjects, and one which was essentially maintained throughout the

experimental period. It would seem, then, that again, whether owing to the heat or to lesser motor restlessness, the oxygen consumption rate (heat production) was slightly lower for the patients than for the normal subjects. It may be mentioned here that this difference was not dependent on variations in nutritional levels, since the matching of pairs was successful.

The rate of evaporation of insensible perspiration fell steadily during the course of the experimental period for both normal and psychotic subjects. The values were somewhat higher throughout for the patients, and a greater decrease in rate was also seen in this group. It would seem, then, that under these conditions the patients perspired more freely than the normal subjects, despite their lower oxygen consumption rate. The more rapid fall in rate in the schizophrenic group is probably to be attributed to their lesser reaction to warmth or their greater degree of relaxation.

TABLE 2.—*Means of Skin and Rectal Temperatures, Oxygen Consumption Rate and Evaporation Rate of 20 Normal Controls and 20 Schizophrenic Patients on Each of Three Observation Periods Under Basal Conditions and After Administration of Dinitrophenol*

		Normal Control Subjects: Observation Period			Patients: Observation Period		
		I	II	III	I	II	III
Temperature, degrees C.							
Thumb	Basal	32.2	32.8	32.8	32.4	32.8	32.5
	Dinitrophenol	33.0	33.7	33.5	32.7	33.0	33.1
Finger	Basal	30.9	32.1	31.7	31.3	31.5	31.1
	Dinitrophenol	33.1	33.5	33.3	32.0	32.3	32.4
Foot	Basal	30.3	30.2	30.2	29.8	29.6	29.4
	Dinitrophenol	30.9	31.8	31.8	29.6	30.2	30.3
Rectum	Basal	36.7	36.6	36.5	36.8	36.7	36.5
	Dinitrophenol	36.7	36.6	36.6	36.8	36.7	36.7
Oxygen consumption rate, per cent.	Basal	93	94	100	89	87	88
	Dinitrophenol	117	125	128	107	111	113
Rate of evaporation of insensible perspiration, Gm. per hr.	Basal	40	37	35	43	39	36
	Dinitrophenol	41	47	53	42	44	46

From the foregoing data, one may say, then, that this group of schizophrenic patients exhibited less reaction to warmth than normal subjects, as shown by a slighter change in the skin temperature and in the oxygen consumption rate and by a greater decrease in the amount of sweating.

In considering the data for the dinitrophenol days, I shall emphasize chiefly the changes from the values for the "basal" days, since the data obtained on these days serve as a base line. Such differences in levels are shown in table 3, for the sake of convenience.

For the normal subjects the values for skin temperature were definitely increased after the administration of dinitrophenol, the effect being noted on the first reading one and a half hours after the ingestion of the drug. The effect on skin temperature was most marked on the finger and had generally achieved its maximum height at the second series of measurements. In the patients the rise in skin temperature was distinctly less over the corresponding points and did not reach the maximum until the last reading, thus indicating not merely a lesser but also a slower reaction.

The rectal temperature in both groups showed no change until the last reading, when a rise of 0.2 C. (0.36 F) was found for the patients, as compared with 0.1 C. (0.18 F.) for the normal controls.

The oxygen consumption rate of the normal subjects was increased from 24 to 31 per cent. The administration of dinitrophenol apparently resulted in a maximum effect at the third reading, the value of which was 128 per cent, but, owing to the sudden increase of the corresponding value to 100 per cent on the "basal" day (table 2), the actual change was 28 per cent, less than that obtained on the second reading.

In the patients the increase due to the medication ranged from 18 to 25 per cent, and was consistently less than that in the normal subjects. It would seem, then, that heat production is stimulated less in patients than in normal controls. The greater reactivity of the normal subjects is further emphasized by the fact that there is a negative correlation between the level of the oxygen consumption rate on the "basal" day and the increase after dinitrophenol. Thus, it would be expected that the patients who had the lower values would theoretically have shown a greater effect from the drug. That they did not makes the results more significant.

TABLE 3.—*Differences Between Mean Values for Dinitrophenol and for "Basal" Days*

	Normal Control Subjects: Observation Period			Patients: Observation Period		
	I	II	III	I	II	III
Temperature, degrees C.						
Thumb	+0.8*	+0.9	+0.7	+0.3	+0.2	+0.6
Finger	+2.2	+1.4	+1.6	+0.7	+0.8	+1.3
Foot	+0.6	+1.6	+1.6	−0.2	+0.6	+0.9
Rectum	0.0	0.0	+0.1	0.0	0.0	+0.2
Basal metabolic rate, percentage	+24	+31	+28	+18	+24	+25
Evaporation rate, Gm. per hr.	+1	+10	+18	−1	+5	+10

* + indicates a mean value higher on the dinitrophenol day.

The sweating mechanisms seem to have been affected later than the oxygen consumption rate or the skin temperature. No change was noted until two and a half hours after ingestion, when the rate of excretion rose to a level of 47 Gm. per hour in the normal subjects, an increase above the corresponding basal level of 27 per cent. The rate of evaporation became progressively greater, the final value reaching 53 Gm. per hour, an increase of 51 per cent.

In the patients, as in the normal subjects, no effect was noted until the second reading. Then an increase of 13 per cent was found, which in the final hour increased to 28 per cent. Thus the increase in rate of evaporation was relatively and absolutely greater in the normal subjects, who, moreover, under basal conditions perspired less than the patients.

COMMENT

A consideration of the foregoing data leads to two conclusions: (1) There are only slight differences between schizophrenic patients and normal control subjects under basal conditions; (2) the patients are definitely less reactive under conditions in which the organism is forced to make adaptive responses. The similarity of the situation to that in

the sympathectomized animal is suggestive. It is probable that the many observations of normal physiologic functions in the schizophrenic patients are due to the data having been obtained under "basal" conditions and that dysfunctions could be more readily detected if the subjects were placed in emergency situations.

The reason for the lack of responsivity of the schizophrenic patient to the stimulus employed is as yet not clear. It is probable, since heat loss and heat production tend to balance each other under these environmental conditions, that the slighter rises in skin temperature and rate of evaporation are due to the lesser increase in heat production. In the last lies the crux of the situation. Dinitrophenol, as Tainter and Cutting [4] have found, is a general metabolic stimulant not dependent on the intermediary activity of any endocrine or nervous structures.

The implication of the results obtained in this study is that the schizophrenic process is not confined to the central nervous system but is widespread throughout the bodily tissues. The point of view may be upheld that the psychologic aspects of the psychosis may explain the physiologic findings, but it seems more reasonable to suppose that the two aspects are different phases of the same pathologic process. Since the patients in this study were all in a chronic stage of the disease, I am unable to make any statements concerning the situation in the more acute phases. This greater resistance to stimulation (which is found with other medicaments, such as thyroid [5] and epinephrine,[6] which involve nervous mechanisms as well) may serve as an explanation for the poor results obtained with therapies.

SUMMARY

A study was made of the skin and rectal temperature, the oxygen consumption rate and the rate of evaporation of insensible perspiration under controlled environmental conditions of 30 C. and 20 per cent relative humidity in 20 normal controls and 20 otherwise healthy schizophrenic patients in a chronic stage of the psychosis. The investigation was carried on under identical conditions on two days, on the first of which no medicament was given and on the second of which 300 mg. of dinitrophenol was administered by mouth to each subject.

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Under basal conditions, the normal subjects showed a distinct elevation of skin temperature, a rise in the rate of oxygen consumption and a slight fall in the rate of evaporation. The patients showed little increase in temperature, no change in the rate of oxygen consumption and a more rapid fall in the rate of evaporation.

After the administration of dinitrophenol, the normal subjects showed an increase in skin temperature up to 2.2 C. (3.96 F.), an elevation in the oxygen consumption rate of 31 per cent and an augmentation in the evaporation rate of 51 per cent. The patients showed less reactivity to the drug, the corresponding changes being 1.3 C. (2.34 F.), 25 per cent and 28 per cent, respectively.

CONCLUSION

In the chronic stage of the psychosis, schizophrenic patients show less reactivity to metabolic stimulation than do normal subjects.

MINERAL CONTENT OF THE BRAIN

CHANGES IN EXPERIMENTAL ANIMALS FOLLOWING INJECTIONS OF INSULIN AND METRAZOL

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The pathologic changes produced by excessive amounts of insulin have been studied extensively by many authors. In man, Wohlwill,[1] Doering,[2] Terplan [3] and others described lesions in the cerebral neurons following hyperinsulinism. Stief and Tokay,[4] Schmid [5] and Weil and we [6] demonstrated the damaging action of insulin on the central nervous system in experimental animals. Reports in the literature of damage to the brain following the administration of metrazol are still scarce. Strecker and his associates [7] and Stender [8] studied the changes occurring after large doses of metrazol in experimental animals. Weil and one of us (E. L.) [9] reported pathologic alterations in brains of rabbits following injection of metrazol over a long period.

According to most authors, there seems to be no doubt that large doses of insulin or metrazol injected over a long period produce severe

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From the Elgin State Hospital.

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irreversible changes in the central nervous system. The question whether the pathologic findings are due to a direct toxic effect or are secondary to interference with the blood supply has not yet been definitely answered. The majority of authors favor the latter view.

It is known that a marked shift occurs in the electrolytes of the blood during insulin coma, as well as during metrazol convulsions. This depends largely on the pronounced metabolic changes and the violent muscular contractions, so that it is not possible to investigate by the usual methods of examination whether the electrolytes present in the central nervous system are affected by insulin and metrazol.

This paper is a study of the mineral content of the ganglion cells of the rabbit brain following administration of insulin and metrazol. According to Weil,[10] normal fresh brain tissue contains about 1 per cent of mineral ash, which consists chiefly of calcium, magnesium, phosphorus, sodium, potassium, iron and chloride. According to this author, there is no significant difference between the amount of inorganic substance in the human brain and that in the brains of cattle.

Since purely chemical methods do not furnish information about the distribution of minerals within the ganglion cells, microincineration was used, a method previously applied to the study of the central nervous system of mammals by Scott.[11] Recently, Alexander and Myerson[12] examined the mineral skeleton of various lesions of the human brain with this method. It permits observation of the distribution of the various minerals, especially calcium, iron, silica, potassium, sodium and magnesium. These minerals may be distinguished by differences in color, but since such a differentiation is subjective and inexact, qualitative analysis was not made in this study. Microincineration has its special value in judging the quantity and distribution of mineral substances in the cell body.

The most highly mineralized structures in the rabbit brain are the large and small pyramidal cells of the cortex, the large pyramidal cells of the cornu ammonis and the granular layer of the cerebellum, while the granular cells of the cortex contain only a comparatively small amount of mineral. The mineral is accumulated in the Nissl bodies and can be seen also in the nucleolus. These structures stand out by their brilliant white and yellowish white color when examined under dark field illumination, while the nucleus appears to be black, indicating that it contains no mineral ash, or only a negligible amount.

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EXPERIMENTS

The experiments were carried out on 23 rabbits. Seven animals received injections of insulin daily, and the resulting hypoglycemic states were interrupted by the administration of dextrose. The total amount of insulin given to the animals varied between 59 and 402 units (see table). After the series of injections the rabbits were allowed to survive for from eleven to one hundred and seventeen days. They were then killed by opening the carotid arteries; the brain was fixed in a solution containing 9 parts of absolute alcohol and 1 part of solution of formaldehyde U. S. P. After the usual embedding in paraffin, sections, 4 microns in thickness, were heated gradually and kept at 650 C. for ten minutes in order to insure complete incineration. Cresyl violet, Bodian and Stern preparations were made for comparative studies. The incinerated sections were examined and photographed under dark field illumination. Four rabbits received metrazol in doses ranging from 2.45 to 21 cc. of a 10 per cent solution, and 3 rabbits were examined after having received insulin and metrazol at the same time. Four animals served as controls.

RESULTS

The accompanying table gives a short survey of the results obtained in these experiments. The ganglion cells in sections of the brains of animals which had

Results of Studies of Mineral Ash Content of Brain Following Insulin and Metrazol Injections

Rabbit No.	Total Units of Insulin	Total Amount of Metrazol, Cc.	Days Treated	Number of Seizures	Days of Survival	Results
8	59	....	65	45	11	Cornu ammonis and cortex: severe hypomineralization, demineralization and some dust formation
35	59	....	3	11	D*	Slight dust formation in cornu ammonis, cortex and Purkinje cells
36	155	....	2	6	D	Cornu ammonis and cortex: demineralization. Beginning dust formation of deeper layers of frontal lobe, of Purkinje and of basket cells
12	207	....	48	19	68	Cornu ammonis: severe demineralization and dust formation. Temporal cortex: hypomineralization and bright glia
63	267	....	36	26 shocks 4 seizures	59	Cornu ammonis: severe demineralization. Purkinje cells: shrunken and severe demineralization
65	323	....	54	52	117	Cornu ammonis and cortex: hypomineralization and demineralization, dust formation, glia cells especially bright. Purkinje cells: dust formation
6	402	....	67	46	80	Cornu ammonis: hypomineralization and dust formation. Frontal cortex: hypomineralization
34	...	2.45	1	6	D	Cerebellum: bright granular layer; Purkinje cells comparatively dark; some dust formation
24	...	16.3	30	22	19	Cornu ammonis: severe demineralization and vacuolation. Cortex: severe hypomineralization
23	...	18.0	38	27	11	Cornu ammonis: severe demineralization and dust formation. Frontal cortex: vacuolation
31	...	21.0	27	24	21	Cornu ammonis (end plate): dust formation. Cortex and caudate nucleus: vacuolation, glia cells especially bright
39	56	2.2	8	5	38	Cornu ammonis and caudate nucleus: vacuolation
38	83	3.4	12	16	38	Cornu ammonis and temporal cortex: slight dust formation and hypomineralization
33	121	6.45	27	40	21	Cornu ammonis: hypomineralization, demineralization and dust formation
37	...	....	..	..	..	Control
40	...	....	..	..	..	Control
41	...	....	..	..	..	Control
50	...	....	..	..	..	Control

* Died during a seizure.

received large doses of insulin appeared darker under a low power lens than the cells of the control animals, indicating apparently a smaller amount of minerals. With a high magnification the cells appeared to be severely diseased. Many of them presented the picture of dust formation: The mineral was not accumulated in the Nissl bodies, as is seen normally, but was distributed homogeneously through the entire cell, giving the impression of a fine powder covering its cut surface. The large pyramidal cells of the cornu ammonis showed severe damage, which appeared also in sections stained by ordinary methods. Dust formation, hypomineralization or complete demineralization was invariably present in the cornu ammonis of all the animals treated with insulin.

The large pyramidal cell layer of the cortex, which is normally highly mineralized, appeared very dark and contained only a few traces of mineral ash. Many

Fig. 1.—Cornu ammonis. Normal distribution of mineral in the large ganglion cells. In this figure and in the accompanying figures, dark field illumination was used.

of the cells were completely demineralized, while most of them showed the changes described as dust formation. The cell bodies of the demineralized cells were outlined only by a thin white ring, representing ash residue at the periphery of the cell. The granular layer of the cerebellum, which usually appears as a bright band, was darker than normal, and similar changes could be seen in the Purkinje cells of the cerebellum. These elements either were completely demineralized or displayed a homogeneous distribution of the mineral content (dust formation). In general, the changes observed seemed to parallel the amount of insulin given and the number of seizures. Rabbit 8, for example, which received only 59 units of insulin but had a large number of seizures, showed severe hypomineralization and demineralization in the cortex as well as in the cornu ammonis. In rabbit 35, however, which received the same number of units of insulin but had only eleven seizures, the changes in the mineral content were less marked.

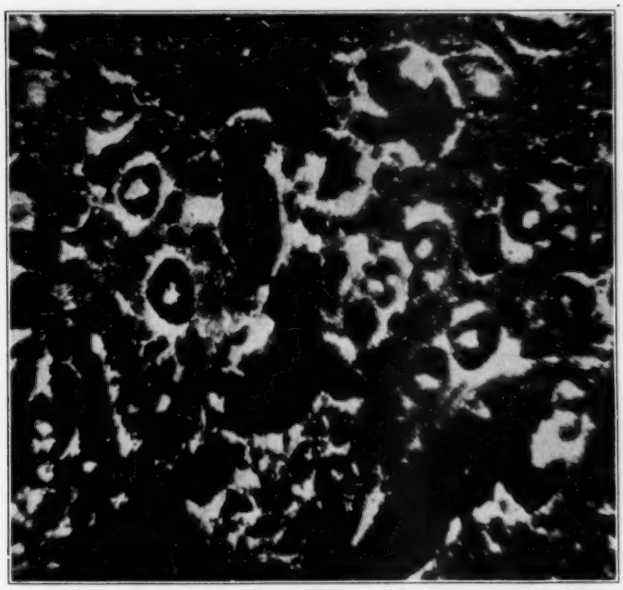

Fig. 2.—Cornu ammonis. Darker appearance of the ganglion cells, with homogeneous distribution of the mineral ash over the cell body (dust formation).

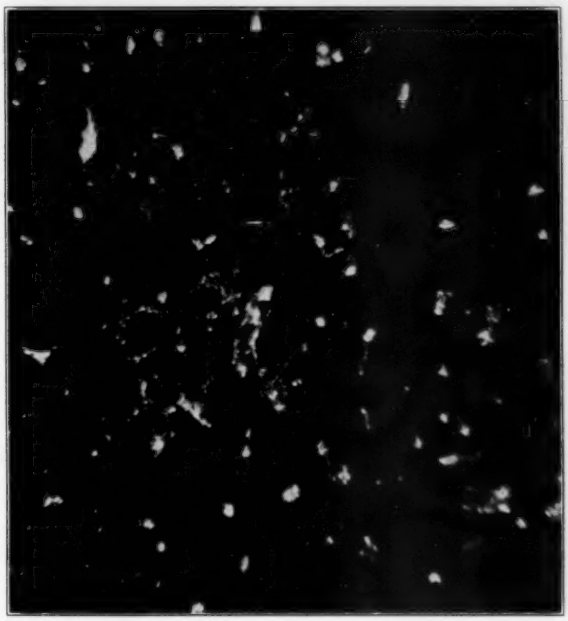

Fig. 3.—Cornu ammonis. Complete demineralization. The cell body is outlined by a thin white ring visible at the periphery of the cell.

In our metrazol series similar changes were observed. It was noted that animals which received a large amount of metrazol showed, besides severe demineralization, marked vacuolation of the ganglion cells. In these vacuolated cells the mineral content was located in only one part of the cell body, which appeared to be comparatively bright, while the remainder of the cell body was black, surrounded by a small white band of mineral ash. The mineral was concentrated in one part of the cell, leaving the rest of the cell body completely demineralized. The changes were most pronounced in the cornu ammonis, which was in accordance with the observations in the Nissl preparations.

The 3 animals which had received injections of insulin and, during the precomatose stage, of metrazol presented changes similar to those already described. In rabbit 39, which received only 56 units of insulin and 2.2 cc. of metrazol and

Fig. 4.—Cornu ammonis. Concentration of the mineral in one corner of the cell body and formation of one or multiple vacuoles.

had only five seizures, there was marked vacuolation of cells in the cornu ammonis and the caudate nucleus. This agrees with comparative Nissl studies of these animals, which showed marked shrinkage, loss of ganglion cells in the cortex and vacuolation of the ganglion cells in the cortex and caudate nucleus. This damage appeared to be much more severe in these rabbits than would have been expected if either drug had been given separately in such small total amounts.

COMMENT

In comparing cresyl violet sections and the microincinerated specimens, it appeared that whenever changes were observed in the Nissl preparation corresponding pathologic alterations could be demon-

strated in the microincinerated section. It is interesting that cresyl violet stains of cells in which dust formation was observed did not present any obvious pathologic damage. It should be emphasized, however, that the Nissl sections were not prepared in the routine manner and that a fair comparison is not possible, since the rapid fixation in the alcohol-formaldehyde mixture produced considerable shrinkage of the tissue. In the three experimental series the glia cells, which usually contain only a small amount of mineral ash, appeared to be much brighter under dark field illumination than normal glia cells, thus possibly indicating that they held an increased amount of minerals. Such an increase in mineral ash was observed by Alexander and Myerson [13] in glia cells in cases of neuronophagia.

The experiments show that during insulin and metrazol seizures a marked shift in the mineral content of the cerebral neurons takes place, which may finally lead to complete demineralization of the ganglion cells. It is questionable, however, whether any of the minerals find their way into the blood stream, where they can be observed by ordinary chemical methods. The shift in the metabolites during the violent muscular contractions following metrazol injections and also in the vehement seizures accompanying insulin shock treatment as seen in the experimental animals, together with severe metabolic changes, is so marked that any change of the minerals in the central nervous system will be completely masked by the shift occurring in the muscle tissue.

In order to determine whether an actual decrease of mineral substances in the central nervous system takes place during hypoglycemic states, the brains of guinea pigs were ashed after more than fifteen insulin convulsions and compared with the brains of normal animals. The normal brains yielded an average of 1.43 per cent of ash residue, and the brains of the hypoglycemic animals, 1.44 per cent. This, together with the microincineration experiments, indicated that there was no actual loss of mineral substance in the brain during hypoglycemic states, but merely a shift from the ganglion cells, probably to the glial apparatus.

Since dust formation of the ganglion cells was observed in dehydrated cats by Alexander and Myerson,[12] it is possible that our pathologic observations are related to a disturbance of water metabolism. The water content of the brains of rabbits and guinea pigs after the animals had been subjected to a large number of hypoglycemic convulsions was compared with that of the brains of normal animals by drying the brains in a vacuum oven. The water present in the brains of both the normal

13. Alexander, L., and Myerson, A.: Minerals in Normal and in Pathologic Brain Tissue, Studied by Microincineration and Spectroscopy, Arch. Neurol. & Psychiat. **39**:131 (Jan.) 1938.

and the hypoglycemic animals amounted to 78 per cent. These observations are in accordance with the statement by Sniffen and Irvin,[14] who reported that the moisture content of the rabbit brain under standard controlled conditions was not altered significantly when hypoglycemia was produced. This does not exclude, however, a shift of water from the extracellular spaces into the cells. That such a change takes place was reported by Yannet.[15] This author showed that in cats "during the period of hypoglycemia water passed from the extracellular spaces into the cells, leading to dilution of the cellular constituents."

The occurrence of irreversible changes after many injections of insulin and metrazol having been observed, it was important to determine whether any change in the mineral content of the cell could be found during and shortly after a single insulin shock and during a single metrazol convulsion. Material for biopsy was obtained by brain punctures through a trephine hole before and at various intervals after the administration of insulin and metrazol. Twenty-two biopsies were carried out on 5 rabbits. During the hypoglycemic state these sections showed marked vacuolation and hypomineralization of the ganglion cells. Other biopsy material obtained forty minutes and eight days later revealed no significant changes in the microincinerated sections. It seemed, therefore, that any alteration of the mineral content during one individual shock is reversible, but that after a long period of injections complete restoration is no longer possible.

In rabbits which received metrazol, sections taken during and two minutes after the seizure appeared to be normal, while material taken ten minutes after the convulsion showed vacuolation and hypomineralization. Thirty minutes after the convulsion the damage apparently had been repaired, because specimens taken for biopsy at this time did not exhibit any pathologic changes.

SUMMARY AND CONCLUSIONS

Microincinerated sections of the brains of rabbits treated with either insulin or metrazol or a combination of the two, by a technic similar to that employed in the treatment of patients with psychoses, showed marked changes in the mineral content of the cerebral neurons. These changes consisted of dust formation, hypomineralization, vacuolation or complete demineralization of the ganglion cells. The changes were prominent in the cornu ammonis, but were also observed in other

14. Sniffen, R. C., and Irvin, D. A.: Physiological Studies in Experimental Insulin and Metrazol Shock, Am. J. Psychiat. **95**:553, 1938.

15. Yannet, H.: Effects of Prolonged Insulin Hypoglycemia and Distribution of Water and Electrolytes in Brain and in Muscle, Arch. Neurol. & Psychiat. **42**:237 (Aug.) 1939.

parts of the brain and appeared to correspond with those in sections stained with cresyl violet. Dust formation and complete demineralization indicated severe damage to the protoplasm and could be observed as long as one hundred and seventeen days after completion of treatment.

Brains of normal and hypoglycemic rabbits and guinea pigs did not present any significant difference in total water content.

Since comparative studies of the brains of normal and of treated guinea pigs did not show any significant difference in the total amount of minerals present, it was thought that there was no actual loss of total ash in the central nervous system.

Experiments in which material was obtained for biopsy during the individual insulin shock and during and at certain intervals shortly after a metrazol seizure showed that changes were present immediately after a convulsive seizure, but that these changes were completely reversible after a certain time.

THE ELECTROENCEPHALOGRAM IN CASES OF NEOPLASMS OF THE POSTERIOR FOSSA

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It is now well established that the electroencephalogram may be used to advantage to locate cerebral lesions through the intact skull (Walter,[1] Case and Bucy [2] and Williams and Gibbs [3]). On the other hand, there is no evidence that deep-lying midline lesions may be localized by this technic, and subtentorial tumors similarly have been reported [4] as not being amenable to localization by the electroencephalogram. More recently Walter [1c] has reported local pathologic alteration in a few cases of cerebellar tumor. The pathologic activity in each of these cases consisted of a focus of slow delta waves appearing "behind the mastoid process" and presumably localizing with respect to the side of the tumor. Additional evidence regarding tumors of the posterior fossa has arisen during our routine electroencephalographic observations on children with various neurologic disorders. Eight patients with neoplasms in this region have thus far been examined. In each of the cases focal pathologic delta waves have been observed in the electroencephalogram posteriorly, presumably over the deeply underlying lesion.

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This work was made possible through the encouragement of and facilities supplied by Dr. Bernard Sachs, when he was Director of the Division of Child Neurology.

1. Walter, W. G.: (*a*) The Location of Tumours by Electroencephalography, Lancet **2**:305-308, 1936; (*b*) The Electroencephalogram in Cases of Cerebral Tumor, Proc. Roy. Soc. Med. **30**:579-598, 1937; (*c*) Critical Review: The Technique and Application of Electroencephalography, J. Neurol. & Psychiat. **1**:359-385, 1938.

2. Case, J. T., and Bucy, P. C.: Localization of Cerebral Lesions by Electroencephalography, J. Neurophysiol. **1**:245-261, 1938.

3. Williams, D., and Gibbs, F. A.: The Localization of Intracranial Lesions by Electroencephalography, New England J. Med. **218**:998-1002, 1938.

4. Walter.[1b] Williams and Gibbs.[3]

METHOD

Observations were made under uniform conditions with the child lying at rest (eyes closed) in a darkened, electrically shielded chamber. The electrodes employed were lead cups, 7 mm. in diameter, which were filled with Sanborn electrocardiogram paste and cemented to the scalp by collodion. Recording was by means of electrodynamic ink-writing oscillographs driven by five stages of conventional push-pull resistance, capacity-coupled amplification. In practice, three unifom independent recording channels were employed simultaneously, usually in modified bipolar combination (Adrian and Yamagiwa;[5] Walter;[1b] figure 1), to locate the focus of any observed pathologic discharge and then to determine the area of its excursion. Careful and repeated checks assured us in each case that the pathologic activity recorded was not due to drowsiness, to electrical gradients resulting from ocular movements or to mechanical distortion of the electrode preparations caused by movements of the head and scalp.

RESULTS

The group of 8 cases to be reported includes 6 cases of cerebellar tumor, 1 of pontile tumor and 1 of tumor of the third ventricle with secondary involvement of the posterior fossa. In 6 of this number examination was made in ignorance of the clinical and roentgenologic findings. In 4 of these 6 patients the findings were verified subsequently at operation. Operation in the fifth and sixth cases was deferred after diagnosis on the basis of unequivocal clinical and roentgenologic evidence. The seventh case was one of known cerebellar neoplasm referred for study after earlier diagnosis by means of a roentgenogram and an encephalogram, and in the eighth case observations were made after partial removal of a large cerebellar neoplasm.

A brief history in each of the 8 cases follows, supplemented in each instance by a summary of the electroencephalographic findings and (in 5 of the cases) by the report of operation.

REPORT OF CASES

CASE 1.—*Astrocytoma of the cerebellum, verified by operation.*

History.—P. C., a boy aged 4 years, was admitted to the hospital Sept. 12, 1938, to the service of Dr. Louis Casamajor, with a history of headaches and vomiting, beginning in November 1936 and increasing in frequency until July 1937. The patient was seen in Mount Sinai Hospital in August 1937, when he presented signs and symptoms of an expanding intracranial lesion. Choking of the optic disks and separation of sutures were present at that time. Hospitalization was advised, but refused. The patient was free from symptoms from September 1937 to April 1938, after which headaches and vomiting recurred. Marked unsteadiness in gait developed in September 1938.

Examination.—The patient was unable to sit unsupported, and tended to fall backward or to the left; he was unable to stand without losing balance; muscle tone in the lower extremities was extremely variable; muscle strength was poor;

5. Adrian, E. D., and Yamagiwa, K.: The Origin of the Berger Rhythm, Brain **58**:323-352, 1935.

the deep reflexes were equal and active; ankle clonus and a Babinski sign were present bilaterally; the abdominal reflexes were absent; papilledema, of 2 D., was present bilaterally; the other cranial nerves were normal; the head was slightly enlarged; the Macewen sign was positive.

Laboratory Examination.—The blood count and results of urinalysis were normal. A roentgenogram of the skull showed separation of sutures, atrophy of the dorsum and posterior clinoid processes of the sella turcica and an appearance of the inner table of the skull suggestive of mild atrophy.

Electroencephalogram.—The electroencephalogram, made on Sept. 16, 1938, showed intermittent slow delta waves, at a frequency of about 2 per second, appearing posteriorly and involving chiefly the occipital lobes. These delta waves showed recurrent foci over both occipital lobes, but were more consistent in appearance and better defined over the left (fig. 1 *A*).

Operation.—Suboccipital craniotomy was performed on September 19. A large astrocytoma, involving the vermis and extending into the left cerebellar lobe, was observed. This was partially removed. The patient's condition became poor

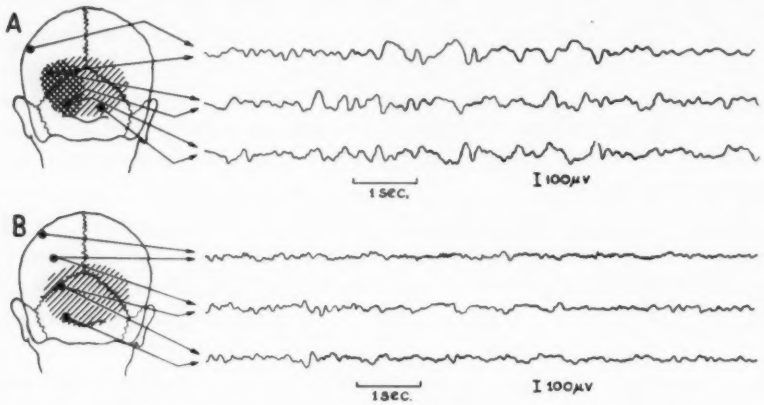

Fig. 1 (case 1).—Astrocytoma of the cerebellum, verified at operation.

A, preoperative tracings showing large delta waves appearing posteriorly. The focus as shown is established consistently between the tracing at the top (parietal leads) and the tracing at the bottom (occipital leads). In this figure and in the following figures, the shaded area in the diagram at the left indicates the total excursion of the focus. Double shading in any instance indicates the area of most consistent focus.

B, six months after operation. The delta waves remain but are smaller in amplitude, indicating some improvement. Note the focus over the left anterior occipital area.

and the procedure was terminated at this point. A second stage operation was performed on September 24, and the remainder of the lesion was removed from the vermis, the fourth ventricle and the cerebellar lobes, the left side being more involved than the right.

Postoperative Course.—The postoperative course was stormy with irregular fever for two weeks. There was stiffness of the neck, and the patient presented the clinical picture of meningitis. Lumbar puncture was performed daily. The fluid was xanthochromic; the total protein content varied from 70 to 140 mg. per

hundred cubic centimeters, and the white cell count ranged from 24 to 1,550 per cubic millimeter. No organisms were found on culture. The patient gradually improved under treatment with sulfanilamide and neoprontosil (the disodium salt of 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′, 6′-disulfonic acid). He was discharged on Dec. 6, 1938.

When seen later, cerebellar signs were still present, with ataxia of all extremities and weakness of both lower extremities. Lumbar puncture was performed every few weeks to reduce the marked bulging in the suboccipital region.

A second electroencephalogram, made on March 16, 1939, six months after operation, showed some improvement. The delta waves were still present and showed foci within a large posterior area, but they were noticeably smaller in amplitude (fig. 1 *B*).

CASE 2.—*Suspected neoplasm of the cerebellum; no operation; clinical improvement after roentgen therapy.*

History.—M. H., a girl aged 6½ years, who was admitted March 30, 1938 to the service of Dr. Casamajor, had been considered well until August 1937, when she showed a tendency to turn the head to the right side, particularly when walking. On Dec. 25, 1937 she complained of generalized headache and suffered several attacks of vomiting. She was free from symptoms for two weeks. Headaches and vomiting then returned, and until the time of admission these attacks became increasingly frequent and severe.

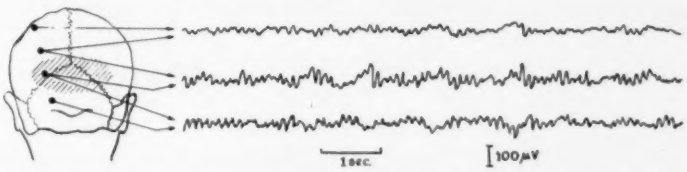

Fig. 2 (case 2).—Suspected neoplasm of the cerebellum; no operation. The delta focus is established approximately over the lambdoid suture. Note normal undisturbed alpha waves superimposed on the slower delta waves.

Examination.—Gait was normal; equilibratory and nonequilibratory tests gave normal results; the deep reflexes were equal and active; no pathologic reflexes were elicited; papilledema, of about 2 D., was present bilaterally; there was limitation of lateral gaze to the left.

Laboratory Examinations.—A blood count showed mild secondary anemia; the urine was normal; the Wassermann reaction of the blood was negative. Roentgenograms of the skull taken on March 31 showed the posterior clinoid processes and dorsum sellae to be somewhat atrophic and the convolutional impressions exaggerated. The impression was that of an unlocalized intracranial tumor.

Course.—A neurosurgeon in consultation expressed the belief that the child had a midline cerebellar medulloblastoma. The signs were relatively few, however, and it was suggested that she be given roentgen therapy, as a therapeutic test, and be closely observed for the development of further signs or symptoms. While in the service the patient contracted mumps, and it was necessary to discharge her on April 19, with the understanding that she be readmitted when her condition was no longer contagious. She was readmitted on June 19, 1938 for high voltage roentgen therapy and possible operation. The clinical condition had improved, and operation was decided against. She was discharged on July 5, 1938 and was studied

at intervals afterward. Her condition improved considerably. The papilledema disappeared, and she returned to school. At present she is leading a normal life. Between May and August 1938 the patient received sixteen high voltage roentgen treatments to the cerebellum and three treatments to the spine.

Electroencephalogram.—On Oct. 14, 1938, recurrent delta waves of low amplitude, at a frequency of 1½ to 3 per second, were observed over the occipital lobes and posterior portions of the parietal lobes. These appeared typically with the normal occipital alpha rhythm superimposed on them, and showed foci over the anterior portions of the occipital lobes (figure 2).

CASE 3.—*Suspected neoplasm of the cerebellum; no operation.*

History.—L. B., a boy aged 5 years, who was admitted on March 12, 1937 to the service of Dr. Casamajor, had shown enlargement of the head at the age of 4 months. At 18 months of age the circumference of the head was said to have been 21½ inches (54.6 cm.). The patient's development was retarded. He did not hold his head up alone until the age of 2 years, and up to the time of admission had been able to speak only single words. Gait was unsteady. There had been no headache, vomiting or visual disturbances.

Examination.—Gait was spastic and ataxic, with a wide base; the reflexes generally were hyperactive; transient ankle clonus was present on the right; no pathologic reflexes were elicited; there was mild ataxia of all extremities; transient,

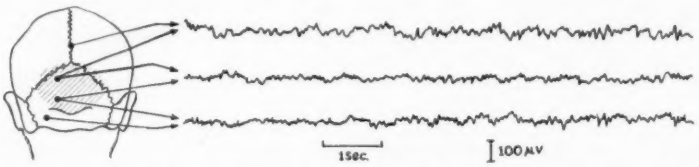

Fig. 3 (case 3).—Suspected neoplasm of the cerebellum; no operation. Tracings were taken with the eyes opened in a semilighted room, since the child would not keep them closed. Note the relatively well defined delta waves showing a phase reversal over the left occipital lobe, whereas the normal alpha waves are largely suppressed. (During brief intervals in which the eyes were closed the normal alpha waves were well defined. See discussion in the text.)

irregular nystagmoid movements of the eyes occurred; the optic disks were somewhat pale; Macewen's sign was positive; the circumference of the head was 21¾ inches (55.25 cm.); the facies was of hydrocephalic character.

Laboratory Examinations.—The blood count and results of urinalysis were normal. Examination of the spinal fluid revealed no cells, a total protein content of 100 mg. per hundred cubic centimeters, a globulin reaction of 2 plus, a colloidal gold curve of 1111110000 and a negative Wassermann reaction.

Roentgenogram of the Skull.—Anteroposterior, posteroanterior and left lateral stereoscopic roentgenograms of the skull showed hydrocephalus; and there was only questionable separation of the coronal suture. The sella turcica was shallow. In the approximate position of the fastigium of the fourth ventricle was a linear streak of calcification, which measured about 2 mm. in width and 1 cm. in length. The impression was that of a midline cerebellar tumor, involving the nodulus.

Encephalogram.—Films taken after the injection of 80 cc. of helium showed the lateral ventricles to be greatly enlarged, and there was some gas in the basal cisterns. The third ventricle, the aqueduct and the fourth ventricle were not

visualized. The findings indicated a tumor in the nodulus of the cerebellum, which was partially blocking the cerebrospinal fluid pathways at the fourth ventricle.

Course.—Consultation with a neurosurgeon resulted in the diagnosis of a neoplasm in the cerebellum, probably an astrocytoma. The patient's family were adverse to operation, as they insisted that his condition was improving. He was therefore discharged on March 24, 1937, to be followed in the outpatient clinic. No new symptoms or signs were elicited at subsequent examinations until the electroencephalogram was taken.

Electroencephalogram.—On Oct. 16, 1938, delta waves, with a frequency of 2 per second, were observed involving chiefly the occipital lobes and the posterior parietal regions. These waves showed intermittent foci within a large area covering most of the occiput (fig. 3).

CASE 4.—*Astrocytoma of the cerebellum, verified by operation.*

History.—V. F., a girl aged 9 years, who was admitted on Dec. 3, 1938 to the service of Dr. Casamajor, had become ill gradually in 1936 with headaches, bifrontal

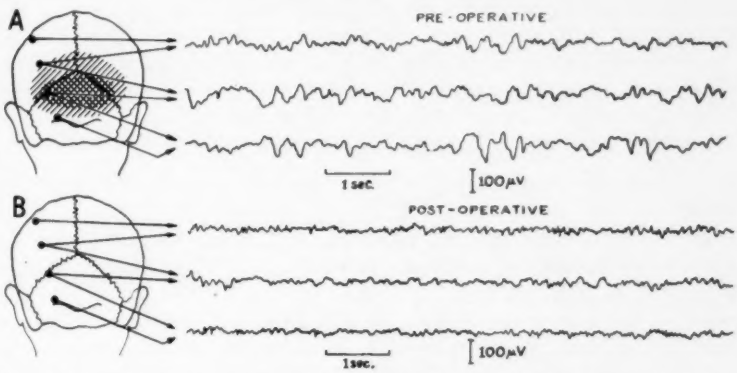

Fig. 4 (case 4).—Astrocytoma of the cerebellum, verified at operation. *A*, preoperative tracings showing well defined delta waves focal over the left occipital lobe. *B*, eleven weeks after operation. There is marked improvement, only traces of the preoperative delta waves remaining.

in location, which became increasingly severe and were soon accompanied by vomiting. Dizziness was also present when the patient arose in the morning. In 1937 vomiting occurred at least three or four times a week. During 1937 the patient also began to show unsteadiness in gait, and this became progressively more marked. In November 1938 the patient became pale and rigid while asleep. She frothed at the mouth, but there were no convulsive movements.

Examination.—The gait was ataxic, with a tendency to fall to the left; there was generalized hypotonia; dysmetria was present on the right in finger to nose tests; there was ataxia bilaterally in heel to knee tests; succession movements were poorly performed on the left; the deep reflexes were greater on the right than on the left in the upper extremities and greater on the left than on the right in the lower extremities; papilledema, of 2 D., was present bilaterally.

Laboratory Examinations.—The blood count and urinalysis gave normal results; serologic reactions were negative. Examination of the spinal fluid revealed 22 white

cells and 1,130 red cells per cubic millimeter and a total protein count of 540 mg. per hundred cubic centimeters. The quantity was insufficient for determination of globulin.

Roentgenograms of the Skull.—There was marked atrophy of the posterior clinoid processes and dorsum sellae, with separation of sutures.

Electroencephalogram.—The tracings, taken on Dec. 6, 1938, showed pathologic alterations in the form of slow delta waves, with a frequency of 2 to 3 per second appearing posteriorly. These waves showed recurrent foci within a large area, which included the anterior portion of both occipital lobes and also extended somewhat into the posterior portion of both parietal lobes. The normal occipital alpha rhythm, with a frequency of 8 to 9 cycles per second, was present but gave evidence of considerable disturbance, appearing typically in brief, poorly defined series of irregular waves, sometimes superimposed on the slower delta waves (fig. 4 *A*).

Operation.—Suboccipital craniotomy was performed on Dec. 16, 1938, with removal of cystic astrocytoma of the left cerebellar hemisphere.

Electroencephalogram.—A second observation, carried out March 4, 1939, eleven weeks after operation, revealed a marked change in pattern. The previously well defined occipital delta waves were now absent. In their place a few slow waves of low amplitude were observed (fig. 4 *B*). The occipital alpha waves remained poorly defined. An interesting feature of the records at this time was a well defined fast rhythm of about 20 per second. This rhythm had been noted occasionally in the preoperative electroencephalogram, but now appeared to be accentuated.

CASE 5.—*Suspected neoplasm of the brain stem; no operation; roentgen treatment.*

History.—V. S., a girl aged 5½ years, who was admitted on Jan. 3, 1939 to the service of Dr. Casamajor, had begun to complain of intermittent frontal headaches on Nov. 27, 1938. On Dec. 7, 1938 she complained of diplopia, and the parents noticed that her eyes were crossed. At this time she also began to experience difficulty in walking. In the middle of December the parents noticed that the patient's face was drawn to the right when she laughed. Since November 1938 she had become progressively "irritable and cranky."

Examination.—The right foot dragged in walking, with a tendency to veer to the left; associated movements in the right arm were decreased; the deep reflexes were increased on the right side, with ankle clonus and a positive Babinski sign; there was limitation of lateral gaze to the left; horizontal and vertical nystagmus were present; there was no papilledema; weakness of the right side of the face of central type was present.

Laboratory Examinations.—The blood count and urinalysis gave normal results; The Wassermann reaction of the blood was negative; examination of the spinal fluid revealed 2 cells per cubic millimeter, a total protein content of 14 mg. and absence of globulin.

Roentgenograms of the Skull.—On Jan. 3, 1939, the films showed nothing abnormal except a small area of decreased density just above the left lesser sphenoid wing, surrounded by an area of increased density. "This was suggestive of a small bone cyst, probably of epidermoid type."

Electroencephalogram.—On January 5 the electroencephalogram showed pathologic slow waves, varying in frequency from 2 to 5 per second, appearing diffusely over both hemispheres. These waves showed noticeable lateralization to the left. Anteriorly, over the sensory-motor areas, the pathologic activity was better defined

and tended to be faster (3 to 5 per second) than posteriorly. Foci for the faster waves were observed over the precentral region, shading from the midline well into the left hemisphere (fig. 5 *A*). Posteriorly, the slow waves had a frequency of about 2 per second and appeared usually with the normal occipital alpha waves superimposed on them. They showed recurrent foci over an area including chiefly the anterior portion of both occipital lobes, but the best defined focus occurred over the left lobe (fig. 5 *B*).

Encephalogram (Jan. 10, 1939).—Films taken after the injection of 60 cc. of oxygen showed a small amount of gas in the basal cisterns and in the cerebral sulci in the frontal region. The callosal sulcus on the left was visualized. At no time was there any gas in the ventricular system. The examination was regarded as unsatisfactory; reexamination was requested.

Ventriculogram (Jan. 25, 1939).—The films showed moderate enlargement of the lateral and third ventricles, the left lateral ventricle being larger than the right. The aqueduct and fourth ventricle were displaced upward and backward, indicating

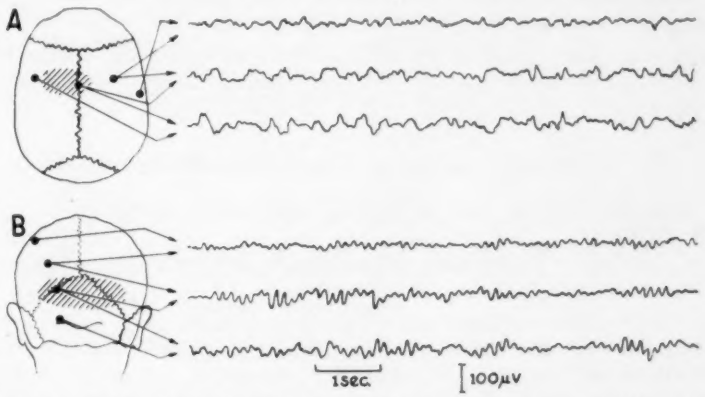

Fig. 5 (case 5).—Suspected neoplasm of the brain stem; no operation. *B* shows the posterior delta focus. Note poor definition of the delta waves. The normal alpha waves are superimposed. *A* shows the additional focus anteriorly, over the left precentral region.

the presence of a mass anterior to these structures. The impression was that of an intracranial tumor, either in the pons or anterior to it.

Course.—Because the neurosurgeon believed that the neoplasm was inoperable, the patient was given high voltage roentgen therapy. While in the hospital her disability in walking became much more marked and bilateral papilledema developed. Mentally, the patient became increasingly apathetic and slow. She was discharged on February 21.

CASE 6.—*Astrocytoma of the cerebellum, verified by operation.*

History.—A. O., a girl aged 7½ years, who was admitted on Oct. 6, 1938 to the service of Dr. Bryon P. Stookey, at 15 months of age had shown tremor, weakness and ataxia of the extremities, with vomiting and periods of unconsciousness. She had been admitted to the New York Post-Graduate Hospital in 1932, where suboccipital craniotomy was performed. A cyst, occupying the region of the vermis of the cerebellum, was removed. The patient's condition was said to have been much improved until four months before admission to the Neurological Institute,

when slight agraphia and ataxia developed. For one month previous to admission she had complained of frontal headache and pain in the upper part of the abdomen.

Examination.—Gait was slightly ataxic; clumsiness was present in heel to knee and finger to nose tests; the reflexes and muscle tone were slightly increased in the lower extremities, more on the right than on the left; no pathologic reflexes were elicited; there was questionable decrease in vibratory sensibility, together with impaired position sense, in the left lower extremity; 2 D. of papilledema, without hemorrhages, was present in both fundi; the pupils were equal and reacted well to light and in accommodation; there was no nystagmus; the other cranial nerves were normal. A suboccipital craniotomy scar was present, with no bulging; the circumference of the head was 45 cm.; Macewen's sign was positive. Systemic examination gave normal results. The patient was mentally alert and cooperative.

Laboratory Examinations.—The blood count was normal; Wassermann and Kline reactions of the blood were negative; examination of the spinal fluid revealed 3 cells per cubic millimeter, a total protein content of 63 mg. per hundred cubic centimeters, a globulin reaction of 1 plus, a colloidal gold curve of 1111000000 and a negative Wassermann reaction.

Operation.—On October 8 secondary suboccipital craniotomy was performed, with subtotal removal of a large cystic astrocytoma involving the right cerebellar hemisphere.

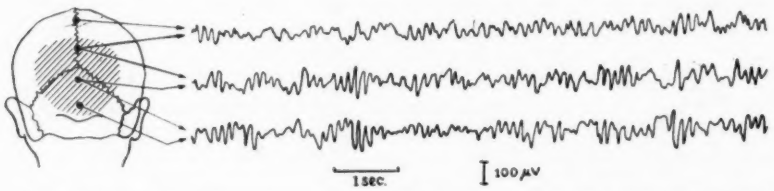

Fig. 6 (case 6).—Astrocytoma of the cerebellum, verified at operation. Tracings taken twelve weeks after partial removal of the tumor and one week prior to recurrence of symptoms. Note delta waves with normal alpha waves superimposed and focal over the occipital lobes (midline).

Postoperative Course.—The course was uneventful, save for considerable bulging in the suboccipital area. The patient was discharged on November 4. She was well until Jan. 12, 1939, when she appeared listless and complained of soreness in the right side of the neck. Her temperature rose to 103 F. She was readmitted January 15. Physical examination revealed cerebellar signs bilaterally, more marked on the right, and there was diminution of all modalities of sensation over the right half of the body. The suboccipital region showed bulging and there was a small pustule in the operative incision. The patient had irregular fever, the temperature reaching 103.4 F. The condition of the wound improved with local treatment, and the fever gradually subsided. The patient was discharged on January 28.

Electroencephalogram.—On Jan. 9, 1939, six days previous to the patient's second admission, slow delta waves, with a frequency of 2 to 3 per second, were observed involving the occipital and parietal lobes. These slow waves appeared consistently with the normal dominant 9 per second occipital alpha waves superimposed on them and exhibited foci with a large area extending well into the parietal lobes (fig. 6).

CASE 7.—*Astrocytoma of the third ventricle, verified by operation.*

History.—B. O., a girl aged 9 years, who was admitted on Jan. 22, 1939 to the service of Dr. Byron Stookey, had had attacks of severe headache accompanied by nausea and vomiting, beginning in January 1936. An attack lasted about two hours, the child becoming progressively more drowsy and finally falling asleep for three or four hours. On awakening she was entirely free from symptoms and remained so until the next attack, which came after an interval of six to eight weeks. During 1937 she was almost entirely free from attacks, but early in 1938 they returned and became progressively more frequent. Except for the aforementioned symptoms, the only complaint was moderate tremor of the hands in executing skilled movements. There were no convulsive phenomena except for one attack in the spring of 1936, while the patient was acutely ill with mumps. Since 1936 a gradual increase in the prominence of the forehead had been noticed.

Examination.—There was a slight tendency for the child to veer to the right while walking; terminal tremor was present in the finger to nose test; the deep reflexes were equal on the two sides; the abdominal reflexes were more active on the left; the Babinski sign was absent; there was 2 D. of papilledema bilaterally; the visual fields were normal; the right pupil was slightly larger than the left; weakness of central type was present on the right side of the face; Macewen's sign was positive; there were prominent frontal bosses.

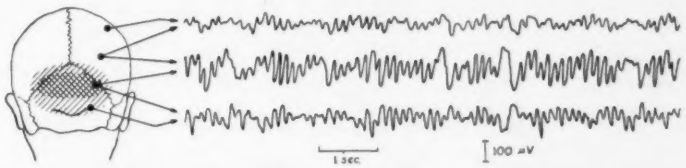

Fig. 7 (case 7).—Neoplasm of the third ventricle compressing structures of the posterior fossa. The normal alpha waves tend to be superimposed on the delta waves, which show phase reversal over the right occipital lobe.

Laboratory Examinations.—The blood count and urinalysis gave normal results; the Kline reaction of the blood was negative; examination of the spinal fluid (ventricular) revealed 2 cells per cubic millimeter, a total protein content of 14 mg. and absence of globulin.

Roentgenograms of the Skull.—The vault was considerably enlarged; convolutional impressions were increased, with separation of sutures; the clinoid processes and dorsum sellae were atrophic.

Ventriculogram.—The films showed marked enlargement of the lateral ventricles and tremendous enlargement of the third ventricle. A tumor occupied the hypothalamic and the ventral portion of the prepineal part of the third ventricle. The aqueduct and fourth ventricle were not visualized.

Electroencephalogram.—On Jan. 30, 1939 intermittent delta waves, with a frequency of 2 to 3 per second, were observed, often with the large normal alpha waves superimposed on them. Foci for these waves were noted within a large area involving chiefly the occipital lobes (fig. 7).

Course.—On February 2, ventriculograms were taken after bilateral posterior trephination with removal of 425 cc. of fluid, which was replaced with oxygen. The films were developed immediately, and right parietal osteoplastic craniotomy was then performed. An approach to the third ventricle was made through the

right lateral ventricle, and a large amount of tumor was removed from the third ventricle. The patient's condition became poor, and it was necessary to terminate the procedure before effecting complete removal. On the evening of February 2 the patient's temperature rose to 108 F., her blood pressure fell, she suffered from several generalized convulsive seizures and died.

Autopsy.—A large tumor occupied the third ventricle and invaded the cephalic portion of the midbrain. There was gross anatomic evidence of compression of the structures of the posterior fossa, the brain stem being displaced downward and backward.

CASE 8.—*Astrocytoma of the cerebellum, verified at operation.*

History.—M. S., a girl aged 4 years, who was admitted on Feb. 6, 1939 to the service of Dr. Casamajor, during the summer of 1938 had tended to hold her head tilted to the left. Toward the latter part of the summer she began to complain of mild frontal headaches. In December 1938 she suffered from severe frontal headaches at night; gradually the headaches began to occur during the

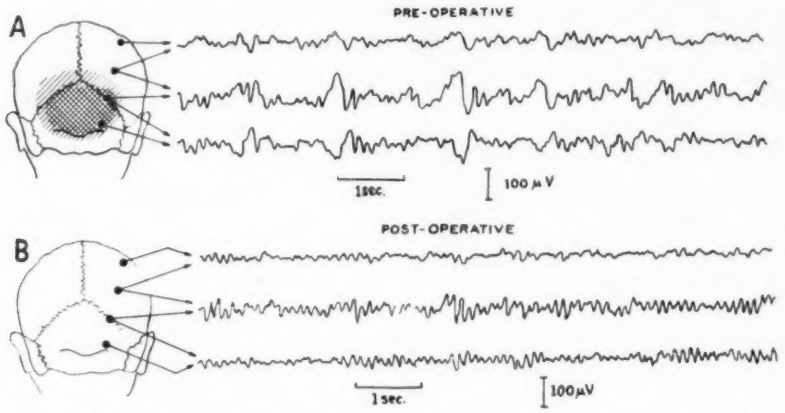

Fig. 8 (case 8).—Astrocytoma of the cerebellum, verified at operation. *A*, preoperative tracings showing large delta waves focal over the right occipital lobe. *B*, seventeen days after operation. Only slight traces of the preoperative delta waves remain. The normal alpha rhythm now dominates the pattern.

day also, so that by the end of December they became so severe that she cried out in distress. Tonsillectomy was performed on Jan. 3, 1939, and the patient was free from symptoms for five to six days, but headaches then returned with increased severity. Vomiting first occurred on January 24. On January 27 the mother noticed for the first time that the patient tended to stagger toward the left in walking. She was admitted to Babies Hospital on February 1, where papilledema of 4 D. was found bilaterally. The patient showed an ataxic gait, and dysmetria and ataxia in nonequilibratory tests. Roentgenograms showed separation of sutures. The spinal fluid contained 2 cells per cubic millimeter and 25 mg. of protein per hundred cubic millimeters. The patient was transferred to the Division of Child Neurology on February 6.

Examination.—The gait was markedly ataxic, with a tendency to veer toward the left; the head was tilted toward the left; there was questionable reduction of strength in the right hand; ataxia was present in the finger to nose and heel to

knee tests; the reflexes were equal but hypoactive: the Babinski sign was negative; there was no gross defect of visual fields; papilledema, of about 4 D., without hemorrhages, was present bilaterally; there was slight weakness of the lower right side of the face, which was more marked on smiling than on active innervation.

Laboratory Examinations.—The blood count and urinalysis gave normal results; the Kline reaction of the blood was negative; examination of the spinal fluid revealed 7 cells per cubic millimeter and a total protein content of 23 mg. per hundred cubic centimeters. The quantity was insufficient for determination of globulin.

Roentgenograms of the Skull.—There were separation of all sutures and slight increase in convolutional impressions; the sella turcica was not definitely atrophic.

Electroencephalogram.—On Feb. 7, 1939 large pathologic delta waves, with a frequency of about 2 per second, were observed over the occipital lobes and posterior areas of the parietal lobes. These waves were most consistently focal over the anterior portions of the occipital lobes, although the area of focus in its total excursion covered most of the occiput (fig. 8 *A*).

Operation.—Suboccipital craniotomy, without air studies, was performed on February 10. A large astrocytoma involving the right cerebellar hemisphere was removed subtotally.

Postoperative Course.—The patient made an uncomplicated recovery from the operative procedure. Clinically, she showed considerable improvement. She still tended to drift slightly to the left, but her gait was less ataxic than formerly. The papilledema disappeared, leaving only slight haziness of the margins of the disks. The apathy which had characterized the patient before operation was no longer present, and she was cheerful and active in the ward. After operation she received a course of roentgen therapy to the cerebellum.

Electroencephalogram.—On February 27, seventeen days after operation, there was marked improvement. Although a few ill defined delta waves were still present and focal over the occiput as before, the pattern was now dominated by a strong normal alpha rhythm (fig. 8 *B*).

COMMENT

Thus far we have observed no cases of neoplasm of the posterior fossa in which the posterior focal delta waves described were not shown. Except in the case of pontile tumor (fig. 5), these slow changes in the posterior region were the outstanding pathologic feature of the picture. In the case of pontile tumor the pathologic alterations were more generalized and lateralized to the side of the enlarged ventricle, and the precentral delta focus was noticeably better defined than the posterior focus. It may also be noted in this case that the posterior delta waves were relatively less well defined than those observed in the cases of cerebellar neoplasms. This fact, together with the presence of the second focus anteriorly, is of interest in view of the location of the lesion deeper in the pons.

The fact that in each instance of tumor of the posterior fossa focal slow waves were shown posteriorly in reasonable anatomic relation to this region is in itself noteworthy. The supplementary evidence in 4 cases in which postoperative examination was made is interpreted as

leaving little doubt that the pathologic activity should be attributed to the lesions demonstrated to be present in this region. The strongest evidence is the clearcut postoperative improvement shown in 2 of the cases (figs. 4 *B* and 8 *B*). In both there was an uneventful recovery. In the third case, although some improvement was noted after operation, there was a definite residuum of delta activity (fig. 1 *B*). The postoperative course in this case was complicated by severe meningitis, probably resulting in additional damage to the brain. The ensuing slow, uncertain recovery (the patient was still ataxic and unable to sit or stand when the electroencephalogram was taken six months after operation) and the pathologic findings in the electroencephalogram were both understandable on this basis. The presence of pathologic alterations in the fourth case (fig. 6) was similarly not unexpected. In this case, in which examination was first made after operation, only part of the tumor had been removed, and in addition there was recurrence of symptoms a few days after the electroencephalogram was obtained.

The slow delta waves observed in cases of cerebral neoplasms have been assumed [4] to arise from damaged tissue adjacent to the lesion, since available evidence (Förster and Altenburger [6]) indicates that intracranial lesions themselves are electrically inactive. Whether comparable damage restricted to the posterior fossa could account for the delta waves observed in the present cases is open to question. Assuming that slow delta activity might be produced in injured neurons of structures in the posterior fossa adjacent to a neoplasm in this region—in neurons of the cerebellar hemispheres, for example—this activity would hardly be expected to survive the long transit through overlying structures in sufficient degree to be recorded from outside the skull. In this connection it is pertinent to note that there is no evidence to indicate that the intact cerebellum contributes to the spontaneous rhythmic patterns recorded in the normal electroencephalogram.

One could possibly account more credibly for the origin of the recorded delta waves more superficially in the occipital lobes. Expansion of a neoplasm of the posterior fossa, through pressure exerted upward against the tentorium, might reasonably be expected to cause some degree of physiologic damage in overlying occipital gray structures. Possible resultant pathologic (delta) alterations in the normal rhythmic (alpha) discharge of these structures would then be more apt to be recorded through the skull than comparable activity arising more deeply in the posterior fossa. Greater or lesser involvement of

6. Förster, O., and Altenburger, H.: Electrobiologische Vorgänge an der menschlichen Hirnrinde, Deutsche Ztschr. f. Nervenh. **135**:277-288, 1935.

the occipital lobes on this basis would plausibly account for the different degrees of pathologic alteration noted in our cases. In case 2, in which marked clinical improvement with high voltage roentgen therapy had been shown, the delta waves appeared merely as elevations of low amplitude in the base line with the normal alpha waves superimposed on them (fig. 2 and page 476). The fact that the alpha rhythm showed little disturbance, together with the low amplitude of the delta waves, suggests that in this case the damage was localized in deeper areas of the occipital cortex and did not significantly involve neurons in more superficial cortical areas, which continued to produce their normal alpha discharge. Radiating from independent deep foci, the delta waves thus appeared as attenuated background changes on which the normal alpha waves were superimposed. In contrast to this picture, one may note the preoperative records in 3 other cases (cases 1, 4 and 8; fig. 1 *A*, 4 *A* and 8 *A*). Here not only were the delta waves larger but they recurrently replaced and disrupted the normal alpha waves. Their greater amplitude and correlative disturbance of the alpha rhythm both suggest more extensive damage to the occipital lobes, with involvement of superficial alpha-producing foci presumably left intact in the previously noted cases. In cases 6 and 7 (figs. 6 and 7) there were presented pictures between the extremes just noted, based probably on intermediate effects of injury to the occipital lobes. In these cases, the delta waves were well defined, but the normal alpha waves were relatively undisturbed. The picture observed in case 7 (fig. 7) is especially interesting in view of the fact that the lesion was primarily in the third ventricle. At autopsy it was observed that while the lesion invaded only the cephalic end of the midbrain, there was anatomic evidence of marked compression of structures of the posterior fossa, the brain stem in particular being pressed downward and backward.[7] The findings in this case are thus not incompatible with the ideas already discussed.

One aspect of the findings which is difficult to evaluate with respect to the assumed origin of the delta waves in the occipital lobes is the response of the latter to opening the eyes. When the eyes were opened the alpha waves were typically abolished, but the response of the delta waves was less predictable. At times they tended to be depressed when the eyes were opened; more often they showed little, if any, apparent change. If records were taken for extended intervals with the eyes open, the delta waves usually came back more prominently than the alpha waves (fig. 3). It may be argued that failure of the delta waves to be uniformly abolished by direct sensory activation of the occipital lobes

7. The neoplasm was also shown to be pressing bilaterally on the optic tracts. Involvement of these tracts in this case (and possibly in the other cases as well) might also be considered as a factor underlying the production of pathologic alterations in the occipital lobes, although it is not clear how this effect might be produced.

is indicative of their origin outside these structures. It appears as reasonable to assume that physiologically depressed neurons in the occipital lobes fail to respond in the normal way to visual stimulation.

SUMMARY

Electroencephalographic findings in 7 cases of neoplasms of the posterior fossa and 1 case of neoplasm of the third ventricle with secondary involvement of the posterior fossa have been presented. In all cases pathologic foci of delta waves were shown posteriorly, primarily over the occipital lobes. Of 3 cases in which examination was made before and after operation, postoperative improvement was clearcut in 2 and partial in 1. Delta waves were present in a fourth case after partial removal of a cerebellar tumor. This patient was examined only a few days prior to recurrence of symptoms. It is suggested that the recorded delta waves were the result of secondary damage to the occipital lobes produced by pressure exerted by the lesions upward through the tentorium.

DISCUSSION

Dr. Leo M. Davidoff, Brooklyn: Regarding the question of the localization of tumors of the brain by means of electroencephalography with reference to the cerebrum, while the combined experience of all workers in this field is still limited, it is generally agreed that there is a great deal of correlation between the abnormal activity as shown in the electroencephalogram and the localization of the lesion. With reference to the cerebellum, there has been less experience, and the general impression was that there was little authentic evidence regarding localization until the work of Smith, Walter and Laidlaw appeared. In spite of the work they presented, I still think it is perhaps safer to be cautious in the interpretation of abnormal waves. My experience with cerebellar tumors has been with adults and not with children, which may account for the difference in the results I obtained. I have studied 5 cases. In 3 of them there was little clinical evidence of increased intracranial pressure; in 2 of these the tumor arose from the eighth nerve and in 1 there was a midline hemangioblastoma. In these 3 cases there were essentially normal records throughout. In the other 2 there was, in addition to cerebellar signs, clinical evidence of increase in intracranial pressure; in these 2 cases there were normal records. In 1 case the abnormal activity was evident throughout; and in the second case the abnormal activity was located anteriorly, and the occipital regions were particularly marked by their normal 10 cycle rhythmicity. This patient proved to have a large midline tumor in the cerebellum.

Dr. Frederic A. Gibbs, Boston: Dr. Williams and I recognized that cerebellar tumors do at times produce localized foci of abnormal activity in other parts of the brain. Such tumors did not in our experience, however, produce foci in the cerebellum. It is exceedingly interesting that the authors have been able to localize so many cerebellar tumors to the occipital region. It should be clear, however, that they have not localized them to the cerebellum. My experience has been similar to that of Dr. Davidoff, namely, that cerebellar tumors occasionally show abnormal foci in other parts of the cerebrum, but such foci may be far removed from the cerebellum; for instance, in a certain case I observed abnormal

foci in the tip of one frontal lobe. Until one can record the electrical activity of the cerebellum it is unlikely that one will obtain better localizations than those which have been presented in this paper. Localization to neighboring structures, if added to other evidence of localizing value, may be of great importance, but it seems likely that the patients dealt with in this report were operated on subtentorially not because of the electroencephalographic localizations but because other types of examination gave adequate evidence of subtentorial localization.

Dr. J. Roy Smith, New York: I certainly agree wholeheartedly with the reservations that have been set forth by both Dr. Davidoff and Dr. Gibbs. Actually, we could not say that we were localizing in the cerebellum the site for the abnormal waves. What we believe we picked up were secondary changes from the occipital lobes; and it is interesting that in the presence of demonstrated lesions in the posterior fossa these pathologic changes did occur and that the primary foci seemed to correspond to the area of origin of the occipital alpha waves.

It does not follow that the presence of this type of slow activity over the occipital lobes is necessarily diagnostic of a lesion in the posterior fossa. Similar pictures may be observed in other types of cases in the absence of lesions in the posterior fossa. All I was presenting here was simply some clinical and electroencephalographic observations. In none of these cases have we made any diagnosis. Our procedure has been merely to examine the case blindly, whenever that was possible, observe the changes and then wait for clinical examination and operation.

I should like to ask Dr. Gibbs whether the patients in his series were adults. It may be that some developmental factor is concerned. It is possible, for example, that the occipital lobes in children may be more susceptible to the type of pressure phenomena that I postulated. I should like to emphasize again that we were not really diagnosing posterior fossa neoplasms; we were merely recording some focal posterior electroencephalographic changes which were associated with these lesions and which were found to be altered after operation.

Dr. Frederic A. Gibbs: My patients were mostly adults.

DISSOCIATION OF DEEP SENSIBILITY AT DIFFERENT LEVELS OF THE CENTRAL NERVOUS SYSTEM

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Although the impulses for the senses of position and vibration are generally regarded as traversing the same nerve pathways, dissociated loss of these modalities has been frequently noted in cases of disease of these tracts.[1] Our study of lesions of the brain and spinal cord producing such sensory disturbances revealed certain interesting observations concerning this dissociation.

1. When dissociation of deep sensibility was found in cases of tumor involving a cerebral hemisphere, position sense was either lost or markedly impaired, while vibratory perception was spared or little affected.

2. When dissociation occurred in cases of neoplasm affecting the brain stem and upper cervical region of the cord, again position sense was severely impaired, while the appreciation of vibration was deficient to a notably lesser degree.

3. With tumors of the thoracic or lumbar region of the cord the converse was true: The vibratory sense was impaired earlier and more severely in the affected lower limbs.

METHODS

Cases of tumor were selected for the study whenever possible because of the localized character of the lesion and the opportunity for verification in each instance by operation or necropsy. Other types of lesions of the brain and spinal cord were studied for comparison. As the study was a clinical one with the aim of furnishing diagnostic aids, the routine methods of neurologic examination were employed. A tuning fork vibrating at 128 oscillations per second was used by all examiners. No special quantitative tests were made.

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1. Laidlaw, R. W.; Hamilton, M. A., and Brickner, R. M.: The Occurrence of Dissociated Disturbances of Pallesthesia and Kinesthesia, Bull. Neurol. Inst. New York **7**:303 (Dec.) 1938.

TABLE 1.—*Data on Patients with Cerebral Tumors Showing Dissociation of Deep Sensibility.*

Name	Age, Yr.	Sex	Type and Location of Lesion	Loss of Position Sense	Loss of Vibratory Sense	Stereognostic Loss	Loss of Discriminative Sense	Comment
M. B.	28	F	Metastatic carcinoma, right parietal and occipital lobes	+++ in left limbs	None	+++ in left hand	+++ in left hand	This is the typical dissociated loss of postural and vibratory sense
B. P.	38	F	Spongioblastoma, right occipital and parietal lobes	++++ in left limbs	+ in left limbs	++++ in left hand	++++ in left hand	Vibratory sense, with pain and temperature sense, was only slightly affected, while loss of postural sense was extreme
S. T.	50	F	Metastatic carcinoma; left parietal and right occipital lobes	++++ in right limbs	+ in right limbs	+++ in right hand	++++ in right limbs	Impairment of position sense and two point discrimination preceded development of astereognosis
A. F.	40	M	Sarcoma, right temporal and parietal lobes	++ in left limbs	None	++ in left limbs	None	After an extensive craniotomy, vibration, together with all other sensory modalities, was involved
A. R.	27	M	Glioma, left parietal lobe	+++ in right toes	± in right toes	None	+++ in right toes	Sensory changes were confined to the right foot, with striking dissociation
V. L.	36	M	Unverified metastatic tumor of brain	++++ in left limbs	± in left limbs	++++ in left hand	++++ in left hand and foot	Sensory changes appeared only after craniotomy
R. C.	34	M	Glioma, right frontal and parietal lobes	+++ in left hand; + left toes	± in left hand	++++ in left hand	++++ in left hand	After craniotomy position sense was completely lost in the left hand, while vibration sense was still comparatively unaffected

RESULTS

Lesions of the Cerebral Hemisphere.—In 21 cases of tumor of the brain in which a satisfactory sensory examination could be carried out and deep sensibility was affected (table 1), marked involvement of position sense was shown in 7, while vibratory perception was comparatively unaffected. In several others there was less pronounced dissociation, but postural disability was never less than the impairment of vibratory sense. When pallesthesia was severely involved, other modalities, that is, touch, pain and temperature, were likewise markedly affected. We found no instances in which the converse was true, that is, in which vibration was deficient while other modalities, particularly the postural sense, were intact. When both postural and vibratory perceptions were involved, without dissociation, the impairment of postural sense preceded that of vibratory sense.

It is well known that with cortical lesions the sense of position, the stereognostic sense and the quality of two point discrimination are often severely involved, while all other modalities are spared. Head and Holmes [2] and Holmes,[3] in an extensive study of sensory disturbances due to lesions of the parietal lobe and thalamus, found marked impairment of postural sense but practically no involvement of vibratory sensation in patients with such lesions. Dandy [4] reported the results in 2 cases of hemidecortication in man. Sensory examination showed that while position sense was completely lost in the affected limbs, vibratory sensation, though diminished, could still be perceived by 1 of the patients. This is a physiologic demonstration of dissociation in a case of a cortical lesion.

Lesions of the Brain Stem and Upper Cervical Region of the Cord.—We had the opportunity to examine 6 cases of tumor of the cervical region of the cord and the brain stem in which deep sensibility in the upper extremities was involved (table 2). Dissociation of the type found with cerebral lesions occurred in 3 of these cases, with postural sense much more involved than vibratory sense.

Examples of dissociation due to lesions of the brain stem are few because deep sensation is seldom involved in such cases. In the syndromes ascribed to occlusion of the posterior inferior and superior cerebellar arteries, position and vibration senses are characteristically

2. Head, H., and Holmes, G.: Sensory Disturbances from Cerebral Lesions, Brain **34**:102 (Nov.) 1911.

3. Holmes, G.: Disorders of Sensation Produced by Cortical Lesions, Brain **50**:413 (Oct.) 1927.

4. Dandy, W.: Removal of Cerebral Hemisphere, Bull. Johns Hopkins Hosp. **53**:31, 1933.

not affected (Spiller;[5] Luhan;[6] Davison, Goodhart and Savitsky[7]). Tumors of the pons likewise produce little involvement of deep sensibility (Alpers and Yaskin[8]). Although neoplasms of the posterior fossa do not ordinarily cause objective sensory disturbances, Cushing[9] and Rubenstein[10] reported cases of astereognosis associated with tumors in the foramen magnum. While postural loss invariably accompanied the astereognosis, vibratory sense and the other sensory modalities were little, if at all, involved. Symonds and Meadows[11] found that loss of

TABLE 2.—*Data on Patients with Tumors of the Brain Stem Showing Dissociation of Deep Sensibility*

Name, Age, Yr., Sex	Type of Location of Lesion	Loss of Position Sense	Loss of Vibratory Sense	Stereognostic Loss	Loss of Discriminative Sense	Comment
M. L. 54 F	Extramedullary schwannoma, 3d to 5th cervical segments	++++ in right hand	+ in right hand	++++ in right hand	++++ in right hand	Slight diminution in touch and superficial perception; after operation position and stereognostic sensory loss recovered completely, while slight impairment of vibratory sense persisted for four months
B. S. 58 M	Meningioma in foramen magnum	+++ in left fingers	None	++++ in left hand	+++ in left hand	Operation for tumor of the parietal lobe. With vibratory sense, superficial pain, touch and temperature senses were spared
B. L. 40 F	Dermoid cyst of foramen magnum	++++ in left hand	None	++++ in left hand	++++ in left hand	Complete dissociation of deep sensibility was again present; position sense, stereognosis and two point discrimination were lost, with preservation of vibration sense and all other modalities

deep sensation was a prominent feature in 6 of 7 cases of compression of the spinal cord at the foramen magnum. They observed that the defect in position sense was much greater in the upper extremities than in the lower. Dissociated loss of the position and vibration senses

5. Spiller, W.: The Symptom Complex of Occlusion of the Posterior Inferior Cerebellar Artery, J. Nerv. & Ment. Dis. **35**:365 (June) 1908.

6. Luhan, J.: Total Contralateral Hemianalgesia in Cases of Vascular Lesions of the Medulla and Pons, J. Nerv. & Ment. Dis. **80**:528 (Nov.) 1934.

7. Davison, C.; Goodhart, P., and Savitsky, N.: The Syndrome of the Superior Cerebellar Artery and Its Branches, Arch. Neurol. & Psychiat. **33**:1143 (June) 1935.

8. Alpers, B., and Yaskin, J.: Gliomas of the Pons, Arch. Neurol. & Psychiat. **41**:435 (March) 1939.

9. Cushing, H.: Notes on a Series of Intracranial Tumors and Conditions Simulating Them [cases 2 and 27], Arch. Neurol. & Psychiat. **10**:605 (Dec.) 1923.

10. Rubenstein, J.: Astereognosis Associated with Tumors in the Region of the Foramen Magnum, Arch. Neurol. & Psychiat. **39**:1016 (May) 1938.

11. Symonds, C. P., and Meadows, S. P.: Compression of the Spinal Cord in the Neighborhood of the Foramen Magnum, Brain **60**:52 (March) 1937.

occurred in 3 of the 7 cases. Loss of vibratory sense was accompanied by gross defects in other sensory modalities.

Lesions of the Spinal Cord.—Of 22 patients with tumors in the lower cervical or thoracic region of the spinal cord in whom deep sensibility in the lower extremities was affected, 9 showed dissociated loss of the vibratory and postural senses, with the vibratory sense the earlier and more severely involved.

Thirty-three patients with non-neoplastic disease of the cord (subacute combined degeneration, 13; myelopathy of undetermined origin, 20) which produced some loss of deep sensibility in the lower extremities

TABLE 3.—*Data on Patients with Tumors of the Spinal Cord Showing Dissociation of Deep Sensibility*

Name, Age, Yr., Sex	Location and Type of Lesion	Loss of Position Sense	Loss of Vibration Sense	Comment
D. R. 25 F	Meningioma, 3d and 4th thoracic segments	None	++++ in toes ++ at malleoli	Superficial pain, touch and temperature sensation were also diminished; after removal of tumor, all sensation became normal
E. S. 63 M	Schwannoma, 6th cervical root	None	+++ in toes +++ in malleoli	Dissociation of deep sensibility marked; advanced age perhaps a factor in loss of vibratory sense
M. R. 55 M	Enchondroma, 6th cervical vertebra	None	+++ in toes ++ at malleoli	During observation, defect developed in vibratory sense, while postural sense remained intact
J. E. 44 M	Extradural lymphoblastoma, 5th and 6th thoracic vertebrae	None	++++ in lower extremities	Instance of extreme dissociation
M. M. 65 M	Hemangioendothelioma at 3d and 4th thoracic segments	None	++++ in toes +++ at malleoli	After removal of tumor, vibratory perception returned in right lower limb
C. B. 63 M	Extruded nucleus pulposus, 11th thoracic vertebra	None	++++ below iliac crests	After operation, sense of vibration returned to normal

were studied. Twenty-four patients showed a predominant disturbance in vibratory sensation, and 9, defects in both modalities. There were no instances in which the postural modality was more deficient than the vibratory, which frequently was the first sense to be involved. In 5 of the 33 patients deep sensibility in the upper extremities was also involved. In all 5 patients the postural sense was more severely affected than the vibratory.

Dissociation of deep sensibility in cases of lesions of the spinal cord has been observed clinically. Woltman [12] and Hamilton and Nixon [13] found in numerous cases of myelopathy associated with

12. Woltman, H. W.: The Nervous Symptoms in Pernicious Anemia: An Analysis of One Hundred and Fifty Cases, Am. J. M. Sc. **157**:400 (March) 1919.

13. Hamilton, A. S., and Nixon, C. E.: Sensory Changes in the Subacute Combined Degeneration of Pernicious Anemia, Arch. Neurol. & Psychiat. **6**:1 (July) 1921.

pernicious anemia that while vibratory sense might be absent in the lower limbs position sense was normal. The converse never occurred. Ahrens [14] concluded that the earliest evidence of involvement of the spinal cord in pernicious anemia was disturbance of vibratory sensibility in the lower limbs. Diminished perception of vibration was rare in the upper extremities, appearing only after profound changes in the lower limbs had occurred. These observations were confirmed in our series of patients with neurologic changes accompanying pernicious anemia.

Gaylord and Howie [15] reported a case of hypernephroma with metastasis to the spinal cord in which sensibility to vibration was lost in a lower limb while position sense was well maintained. In aged persons diminution of vibratory sensation without impairment of position sense is a common finding, as pointed out by Pearson.[16] This instance of dissociation of the vibration and the position sense is attributed to arteriosclerosis of the lumbar region of the cord.

A remarkable instance of dissociation has been noted by Davison and Wechsler,[17] who recorded 2 cases of amyotrophic lateral sclerosis in which, in addition to the usual manifestations of lesions of the pyramidal tracts, there was clinical and anatomic evidence of involvement of the posterior columns. The first patient had marked impairment of position sense in the fingers, with astereognosis and faulty two point discrimination, while vibration sense was spared. The lower extremities were not involved. Histologically there was demyelination of the posterior columns at the first and second dorsal segments, with the fasciculus cuneatus more involved than the fasciculus gracilis. The sensory findings in the second case were confined to loss of vibratory sense in the lower extremities, while the sense of position was intact.

COMMENT

The nature of vibratory sensibility has long been a subject of controversy. It is questioned whether it is a specific sensory modality or, as in the opinion of Symms [18] and Pollock,[19] merely the apperception

14. Ahrens, R. A.: Neurologic Aspects of Primary Anemia, Arch. Neurol. & Psychiat. **28**:92 (July) 1932.

15. Gaylord, J. B., and Howie, J. W.: Brown-Séquard Syndrome: A Case of Unusual Etiology, J. Neurol. & Psychiat. **1**:301 (Oct.) 1938.

16. Pearson, G. H. S.: Effect of Age on Vibratory Sensibility, Arch. Neurol. & Psychiat. **20**:482 (Sept.) 1928.

17. Davison, C., and Wechsler, I. S.: Amyotrophic Lateral Sclerosis with Involvement of the Posterior Columns and Sensory Disturbances: A Clinical Study, Arch. Neurol. & Psychiat. **35**:229 (Feb.) 1936.

18. Symms, J. L. M.: Method of Estimating "Vibratory Sensation," Quart. J. Med. **11**:33 (Oct.) 1917.

19. Pollock, L. J.: Vibration Sense, Arch. Neurol. & Psychiat. **37**:1383 (June) 1937.

of repetitive stimuli of touch and pressure. Pollock showed that after section of the sensory root of the fifth nerve vibratory stimuli could still be perceived on the affected side of the face and tongue. These vibrations had a much lower frequency of oscillation. Preservation of this type of vibration sense after elimination of epicritic and protopathic conductors indicated that pallesthesia is dependent not on certain specific end organs but on the receptors which had not been destroyed by the nerve section. Gilmer [20] determined the points of deep pressure sensitivity over the body and found that it was only these areas which gave a sensation of vibration to electrical stimulation with alternating current. When the electrode was applied to nearby spots, no feeling of vibration other than a burning sensation was experienced, thus indicating the close relationship between pressure and vibratory sensations.

The sense of position, on the other hand, is a well defined modality. Impairment of position sense in cases of cortical tumors is usually accompanied by astereognosis and faulty two point discrimination. These modalities are concerned with appreciation of spatial relationships; they require a fine degree of motor integration and have a large cortical representation. On the other hand, the sense of vibration, or the modalities composing it, in man is hardly concerned with spatial relationship and accordingly does not suffer as much from cortical lesions. In the cases of tumors of the brain studied in which vibratory sensation was considerably diminished, there was also marked involvement of other sensory qualities. In the case reported by Dandy, in which both position and vibration sense were lost, without dissociation, there was marked involvement of all other sensory modalities.

It is evident that the types of dissociation described differ at various levels of the nervous system. Lesions at the level of the thoracic portion of the cord caused greater involvement of vibratory sensation in the lower limbs, while compression of the brain stem and of the upper cervical region of the cord affecting deep sensibility in the upper extremities gave the opposite type of dissociation, namely, marked defect in postural sense, often with little involvement of vibratory perception. It was also noted that when sensory dissociation occurred in the lower extremities as a result of a tumor in the parietal lobe or the foramen magnum, position sense was the modality involved, in contrast to the findings in the lower extremities when the lesion was in the thoracic region of the cord.

These differences in dissociation may be due to the differences in structure and connections of the posterior columns at the different levels. Although both lie in the dorsal funiculi, the pathways of kinesthetic

20. Gilmer, B. von H.: The Relation of Vibratory Sensitivity to Pressure, J. Exper. Psychol. **21**:456 (Oct.) 1937.

and of pallesthetic sensation to the thalamus and cortex are probably not identical. In the lower thoracic and lumbar regions the posterior white columns are composed of the fasciculus gracilis alone, and, especially at the lumbar levels, the volume of white matter is small as compared with the mass of gray matter. In the upper thoracic and cervical segments the dorsal columns are made up chiefly of the prominent fasciculus cuneatus, representing the upper extremities, and the mass of white matter is large.

Fibers from the posterior column, as they approach the medulla, project in two directions. One group, after making synapses in the gracile and cuneate nuclei, ascend to the thalamus in the medial lemniscus, while another bundle, derived principally from the fasciculus cuneatus, travels to the external cuneate nucleus in the medulla, which, in turn, makes connections with the vermis of the cerebellum through the inferior cerebellar peduncle.[21] The external cuneate nucleus, or Clarke-Monakow nucleus, is the lateral portion of the cuneate nucleus. It differs in structure from the internal part, containing larger and more varied cells. These cells resemble those in Clarke's column, which is present only in the thoracic and lumbar regions of the cord. The Clarke-Monakow nucleus is thus regarded as the homologue of Clarke's column (Pass[22]); both are important proprioceptive centers. Fibers from Clarke's column give rise to the dorsal spinocerebellar tract, which accompanies fibers from the external cuneate nucleus to the cerebellum in the inferior cerebellar peduncle.

Ferraro and Barrera[23] found in monkeys that the proprioceptive loss in the upper extremities following lesions of the fasciculus cuneatus in the cervical region was more severe than the postural defect in the lower limbs after section of the fasciculus gracilis at the thoracic or lumbar level. This was explained by the authors as a result of the involvement at the cervical level of fibers traveling both to the medial lemniscus and to the cerebellum. Injury to the dorsal columns at the lower levels affected only the fibers destined for the medial lemniscus, as the cerebellar component representing the lower extremities is conducted chiefly in the intact spinocerebellar tracts.

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21. (*a*) von Monakow, C.: Neue experimentelle Beiträge zur Anatomie der Schleife, Neurol. Centralbl. **4**:265, 1885. (*b*) Mussen, A.: Experimental Investigation of the Cerebellum, A. Research Nerv. & Ment. Dis., Proc. **6**:381, 1926. (*c*) Ranson, S. W.: The Anatomy of the Nervous System, ed. 5, Philadelphia, W. B. Saunders Company, 1936. (*d*) Ferraro, A., and Barrera, S. E.: Posterior Column Fibers in Monkeys, J. Comp. Neurol. **62**:507 (Oct.) 1935.

22. Pass, I. J.: Anatomical and Functional Relationship of the Nucleus Dorsalis (Clarke's Column), Arch. Neurol. & Psychiat. **30**:1025 (Nov.) 1933.

23. Ferraro, A., and Barrera, S. E.: Summary of Clinical and Anatomical Findings Following Lesions in the Dorsal Columns of Macacus Rhesus Monkeys, A. Research Nerv. & Ment. Dis., Proc. **15**:371, 1934; footnote 21 *d*.

Dissociation of position and vibratory senses may perhaps be accounted for on this basis. While position sense may depend on a dual pathway, vibration sense probably has little cerebellar representation, being carried directly to the thalamus in the medial lemniscus. In cases of lesions of the thoracic part of the cord, if only the fibers in the fasciculus gracilis destined for the medial lemniscus are injured and the cerebellar component, presumably carried in the spinocerebellar tracts, is spared, one might expect vibratory sensation to suffer more than postural sense. In this connection an important and interesting observation was made by Putnam [24] in man after incising the posterior median sulcus and commissure in the cervical region for relief of pain. The resultant injury to the fasciculus gracilis produced loss of vibration sense in the lower extremities but no change in position sense. Sensation was undisturbed in the upper extremities. With neoplasms of the posterior fossa involving chiefly the laterally situated cerebellar connections in the inferior cerebellar peduncle, position sense in both the upper and the lower limbs would be more affected than vibration sense, traveling comparatively unhindered through the medial lemniscus, despite compression of the posterior columns

The exact role of these two components in the maintenance of position and stereognostic senses and their relationship to each other, however, are not clear. Lesions confined to the cerebellum, according to Holmes,[25] produce no defect in position sense. Two cases of thrombosis of the anterior spinal artery in the medulla, with destruction of the medial lemniscus, were reported by Davison.[26] In each there was loss of postural, vibratory and stereognostic senses and two point discrimination in the affected extremities. Thus it appears that complete interruption of the medial lemniscus will abolish deep sensation, while a single lesion of the cerebellar pathway will not.

The phylogenetic development of the posterior columns, reviewed by Ariëns Kappers and his associates,[27] furnishes significant correlations. In fishes the vibrations of the water are perceived by the lateral line organs. By appreciation of these periodic changes in pressure the animal can avoid danger and exist in its environment. The dorsal white

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24. Putnam, T. J.: Myelotomy of the Commissure, Arch. Neurol. & Psychiat. **32**:1189 (Dec.) 1934.

25. Holmes, G.: The Croonian Lectures on the Clinical Symptoms of Cerebellar Disease and Their Interpretation, Lancet **1**:1177 (June 17); 1231 (June 24) 1922; **2**:50 (July 8); 111 (July 15) 1922.

26. Davison, C.: Syndrome of the Anterior Spinal Artery of the Medulla Oblongata, Arch. Neurol. & Psychiat. **37**:91 (Jan.) 1937.

27. Ariëns Kappers, C. U.; Huber, G. C., and Crosby, E. A.: The Comparative Anatomy of the Nervous System of Vertebrates, Including Man, New York, The Macmillan Company, 1936, vol. 1.

columns of the spinal cord of fishes are very small. In the higher animals, in which vibratory sensation is of much less importance, the posterior columns, especially those representing the upper limbs, increase in size enormously, the development paralleling the acquisition of the proprioceptive qualities necessary in terrestrial surroundings. There is also a marked progressive accumulation of the dorsal white matter in the cervical portion of the cord, as compared with that at the lower levels, even after allowing for representation of the lower extremities in the fasciculus gracilis at the cervical level. In man this may be correlated with the highly developed, fine kinesthetic, discriminative and stereognostic modalities in the upper extremities used for the performance of intricate movements.

In conclusion, whatever may be the anatomic or physiologic explanation for the dissociation of pallesthesia and kinesthesia, we wish to call attention to the fact that the type of dissociation varies at different levels of the sensory pathways.

SUMMARY

1. Dissociated loss of postural and vibratory sensation was found to be not uncommon with lesions of the cerebrum, brain stem and spinal cord.

2. In 7 patients with cerebral lesions causing disturbance of deep sensibility, position sense, stereognosis and two point discrimination were lost or markedly diminished, while the appreciation of vibration was spared or slightly affected. There were no instances in which the converse was true.

3. With lesions at the thoracic and lumbar levels of the cord the opposite type of dissociation was found. Vibratory sense in the lower extremities was affected earlier and more severely than was the sense of position.

4. In 3 patients with compression of the cervical region of the cord and medulla, with dissociated loss of deep sensation involving the upper extremities, sense of position was more affected than that of vibration, again with astereognosis.

5. The relationship between the clinical disturbances and the structure, function and development of the posterior columns is discussed.

SECTION OF THE DESCENDING SPINAL ROOT OF THE FIFTH CRANIAL NERVE

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AND

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PHILADELPHIA

One of the chief objections to section of the posterior root of the fifth cranial nerve for relief of tic douloureux or facial pain from a maligant growth is the loss of touch sensation as well as the appearance of subjective numbness in the face following this procedure. This disadvantage is common to both the Spiller-Frazier and the Dandy operation. It has been overcome by the technic of Sjöqvist in sectioning the bulbospinal root of the fifth cranial nerve. Ranson and Kuntz [1] had suggested such a procedure in 1931. Sjöqvist, without knowledge of this idea, performed this operation, which he called tractotomy, for the first time and made a preliminary report in 1937. In 1938 he published a monograph [2] in which he gave further proof of the practicable and physiologic basis of this method.

TECHNIC

The technic of the operation, as described by Sjöqvist and performed by us, is essentially as follows: A unilateral exposure of the posterior fossa (fig. 1) is made. The dura is opened, and the cisterna magna is drained. The tonsil of the cerebellum is retracted upward, exposing the vagus roots as they emerge from the medulla oblongata, dorsal to the olivary eminence. An incision is made in the medulla to a depth of 3 to 3.5 mm., at right angles to the axis of the brain stem and on a level with the last caudal filament of the vagus nerve, beginning 1 mm. dorsolateral to the filament and ending 4 to 5 mm. dorsal to it. The section

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From the Neurosurgical Service of the Hospital of the University of Pennsylvania.

Read at the Sixty-Fifth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 7, 1939.

1. Ranson, S. W.: Cutaneous Sensory Fibers and Sensory Conduction, Arch. Neurol. & Psychiat. **12**:1122 (Dec.) 1931. Kuntz, A., in discussion on Ranson.

2. Sjöqvist, O.: Studies on Pain Conduction in the Trigeminal Nerve: A Contribution to the Surgical Treatment of Facial Pain, Helsingfors, Mercators Tryckeri, 1938.

is so placed that it avoids the restiform body and the nucleus of Burdach dorsally and the inferior olivary body ventrally. It is sufficiently caudal to spare the vagal fibers.

Sjöqvist's results in a series of almost 20 patients have proved the premise that pain and temperature sensations are lost in the entire distribution of the fifth nerve while touch sensation is preserved. Further support of this premise has been added by the experiences of Kessel,[3] in 1 case; of Rowbotham,[4] in 3 cases, and of Jackson and Ironside,[5] in 1 case.

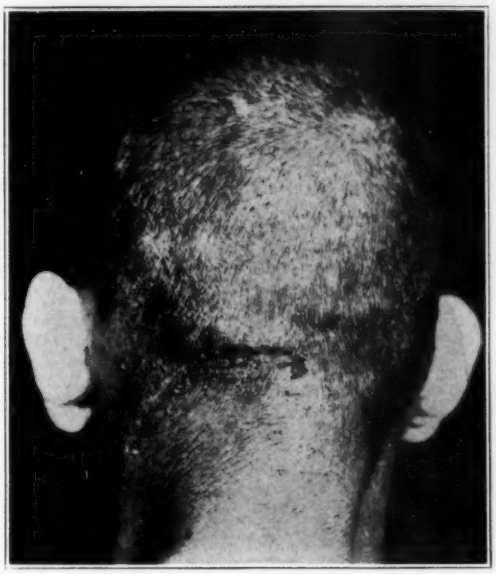

Fig. 1.—Photograph of a patient taken after tractotomy, showing the location of the scar.

MATERIAL

Recently 12 patients (table 1) have been operated on according to the technic of Sjöqvist in the Hospital of the University of Pennsylvania. Four patients were subjected to the operation for trigeminal neuralgia, and the other 8, for intractable facial pain caused by malignant tumors. The operation in 2 instances was com-

3. Kessel, F. K.: Ueber die Behandlung der Trigeminusneuralgie, München. med. Wchnschr. **85**:977, 1938.

4. Rowbotham, G. F.: Treatment of Pain in the Face by Intramedullary Tractotomy, Brit. M. J. **2**:1073, 1938.

5. Jackson, H., and Ironside, R.: Left Trigeminal Pain Treated by Sjöqvist's Medullary Trigeminal Tractotomy, Proc. Roy. Soc. Med. **32**:219, 1939.

bined with section of the upper cervical roots because of extension of the tumor into the area supplied by these roots and in another, with section of the ninth nerve. The results in each of the 12 patients were satisfactory.

TABLE 1.—*Data on Twelve Patients Subjected to Section of the Descending Spinal Root of the Fifth Nerve*

Case	Name	Age, Yr.	Sex	Diagnosis	Duration, Yr.	Location	Character of Pain
1	R. A.	49	M	Trigeminal neuralgia, left	2	II and III	Paroxysmal
2	E. von B.	56	M	Trigeminal neuralgia, right	2	II	Paroxysmal
3	M. T.	63	F	Trigeminal neuralgia, left	1	III	Paroxysmal
4	J. E.	74	M	Trigeminal neuralgia, right	1	II and III	Paroxysmal
5	J. K.	60	M	Carcinoma of jaw, left	2	II	Severe, continuous
6	A. M.	73	M	Carcinoma of jaw, left	..	III	Severe, continuous
7	H. H.	55	M	Carcinoma of jaw	1	II and III	Severe, dull
8	H. V. W.	65	F	Carcinoma of antrum, left	Recent	II	Some, not severe
9	A. W. P.	51	F	Tumor of parotid, left	..	II and III	Mild, continuous
10	E. P.	31	M	Metastasis to preaural glands	..	II and III	Sharp, shooting
11	J. G.	70	M	Carcinoma of maxilla, left	1	II and III	Severe, burning
12	W. S.	53	M	Tumor of maxilla, left (not found)	½	II	Mild, throbbing, preventing sleep

TABLE 2.—*Sensitivity in All Three Trigeminal Divisions of the Fifth Cranial Nerve After Tractotomy*

	Absent	Reduced	Not Evaluated	Normal
Touch sensation	..	8	2	2
Corneal reflex	7	3	..	..
Pain and temperature	10	2	..	..
Lips spared	..	1	..	..
Lip and tongue spared	..	4	..	..
Dissociation of pain and temperature	..	2	..	..

RESULTS OF POSTOPERATIVE SENSORY EXAMINATIONS

Pain.—Pain sensation, as determined by pinprick under a pressure of up to 40 Gm., was completely abolished in the distribution of all three divisions of the trigeminal nerve in 10 of the 12 patients (table 2). One patient had complete analgesia in the area supplied by the first division and partial loss in the areas supplied by the second and third divisions. A zone limited by the nasolabial fold and including the lip was sensitive to pinprick under a pressure of 40 Gm. The remaining area of the second and third divisions required a pressure of only 30 Gm., while the upper cervical segments responded to a pressure of 10 Gm. In another patient the second and third divisions were completely analgesic, and the first division was entirely spared. In 4 patients the tongue, and in 3 the lip, was spared.

Corneal Reflex.—After the operation the corneal reflex was absent in 7 patients, reduced in 3 and normal in 2 (table 2). Corneal sensation to touch with graded hairs was normal or decreased up to a pressure of 8 to 10 Gm. per square millimeter. Sensitivity to such pressures was interpreted by the patient as itching or as vague touch sensation without disagreeable character. Three patients interpreted a pressure of 20 Gm. per square millimeter as painful. In all patients spontaneous winking was unaffected and was equal on the two sides.

Temperature Sensation.—The loss of temperature sensation as a rule corresponded closely with that of pain sensation. The majority of patients were unable to differentiate clearly between boiling hot and ice-cold water. However, in all 10 patients the application of cold or heat produced vague temperature sensation. Most of the patients felt these extremes of temperature as lukewarmness. When cold was applied immediately after heat or in the reverse order, a minimal degree of difference was appreciated. In 2 patients there was dissociation between the preservation of temperature and the abolition of pain sensation. In 1 patient the sensation for heat was fairly well preserved, while cold was felt as lukewarmness.

Touch Sensation.—Touch sensation was grossly preserved, and subjective numbness was absent in all but 2 patients who had received an injection of alcohol

TABLE 3.—*Touch Sensations After Tractotomy*

Number of touch points decreased	6
Threshold of touch points elevated	4
Slight subjective numbness	1
Touch sense not evaluated	2

previous to operation (table 3). However, examination with graded hairs revealed that in 6 patients the number of touch points per square centimeter was decreased, but that the points preserved had a normal threshold. In 4 other patients the threshold for the touch points was increased, and in 2 this increase was combined with a certain loss in the number of touch points. In 1 patient the reduction of touch sensation was sufficient to cause slight subjective numbness. In no patient was qualitative disturbance of touch sensation demonstrated.

Sensations for deep pressure and vibration, as well as those for taste and smell, were normal in all patients.

In brief, therefore, the essential result of the sensory examinations in these patients was loss of pain and temperature sensation in the area supplied by the fifth cranial nerve, accompanied by decrease or loss of the corneal reflex in the majority of the patients. Touch sensation was grossly preserved. No patient actually complained of subjective numbness.

COMPLICATIONS FOLLOWING TRACTOTOMY

Various complications as a result of the operation have been described in the literature. These are: paralysis of the recurrent portion of the laryngeal nerve, headache, nystagmus, difficulties in

swallowing and micturition and ataxia. Of these complications (table 4), we have seen nystagmus in 2 patients and ataxia in 3 patients, as reported by Rowbotham, difficulty in swallowing for a few days after the operation in 1 patient and as unreported signs, intermittent hiccup and nausea in 1 patient.

In 1 of the patients with transient ataxia cooperation and intelligence were sufficient to make possible a detailed sensory examination. The ataxia was demonstrated in the finger to nose test and in rapid associated movements. It was confined to the ipsilateral arm. This patient had a marked decrease in touch sensation in the hand, with a circular limit around the wrist. In this area two point discrimination was impaired and position sense lost. The combination of ataxia and this definite disturbance of sensitivity led us to believe that the nucleus of Burdach

TABLE 4.—*Complications of Tractotomy*

Transient brachial ataxia	3
Transient nausea and hiccup	1
Difficulties in swallowing	1
Difficulties in micturition	0
Paresis of recurrent laryngeal nerve	0
Nystagmus	2

had been injured. The other 2 patients with ataxia were too uncooperative for detailed sensory examination during the time the ataxia was present.

COMMENT

The dissociation of sensation which resulted in some patients from section of the bulbospinal root of the fifth cranial nerve at the level of the junction of the middle and the lower third of the inferior olive permits a discussion of the sensory pattern of the spinal root. All of Sjöqvist's patients retained the sensation of touch. This observation was confirmed by our own results, in that 11 of the 12 patients grossly showed preservation of touch sensation. In the patient for whom the results were at variance, the nucleus of Burdach, in our opinion, had been damaged as a result of an error in technic.

The fact that touch is preserved after tractotomy is in accordance with clinicopathologic observations of authors from Wallenberg on. Sjöqvist confirmed by fiber analysis the premise that the majority of touch fibers remain in the cephalic portion of the nucleus and do not enter the descending portion of the bulbospinal root.

Sensations of pain and temperature, on the other hand, are abolished if section of the descending root is complete. In 1915 Spiller [6] made

6. Spiller, W. G.: Remarks on the Central Representation of Sensation, J. Nerv. & Ment. Dis. **42**:399, 1915.

the statement that even the pathways for pain and temperature sense might be dissociated in the spinal nucleus of the fifth cranial nerve. Sjöqvist and Jackson and Ironsides obtained evidence that in some instances after the spinal root had been sectioned the degree of loss of temperature sense in the face was greater than that of pain sense, and that the reverse was true. In our observations, a vague, indefinite thermal sense, different from tactile sense, was perceived by all the patients, including a patient who had complete loss of pain sense. In 2 of our patients pain sensation was completely lost, whereas temperature sensation was normal. In 1 patient sensation for heat was appreciated, whereas cold was described as "lukewarm." These observations confirm Spiller's concept that not only pain and temperature sensations, but also hot and cold sensations, are represented in separate pathways.

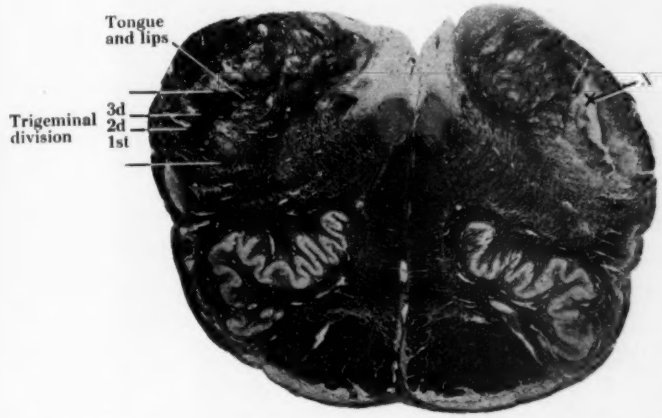

Fig. 2.—Transection of the medulla oblongata at the level of section (*X*) of the right descending trigeminal root.

We conclude, therefore, that the bulbospinal root of the fifth cranial nerve at the level of the junction between the middle and the lower third of the inferior olive contains primarily fibers for pain and temperature sensations but no fibers for deep pressure sense. A few fibers representing touch are probably conveyed by this portion of the root.

Arrangement of the Three Divisions of the Fifth Cranial Nerve in the Descending Bulbospinal Root.—Anatomically, the descending root of the fifth cranial nerve appears in a cross section of the medulla as a crescent (fig. 2). The investigations of Winkler and other anatomists seem to indicate that the fibers of the third division are situated dorsally in the crescent, with the fibers for the tongue and lip at its superior medial tip, the fibers of the first division ventrally and the fibers of the second division between the two.

The results of the partial transection of the descending root in our patients verifies this anatomic concept. In 1 patient the first division was completely spared, while the areas of the second and third divisions were analgesic, with the exception of both the tongue and the lips, which were hypalgesic (fig. 3). In another patient (fig. 4) analgesia was complete in the first division only and partial in the second and third divisions, and an "onion skin" hypalgesia was present around the upper lip and the mouth, similar to that which has been described in cases of bulbar lesions of the nucleus of the fifth cranial nerve. Hypalgesia in

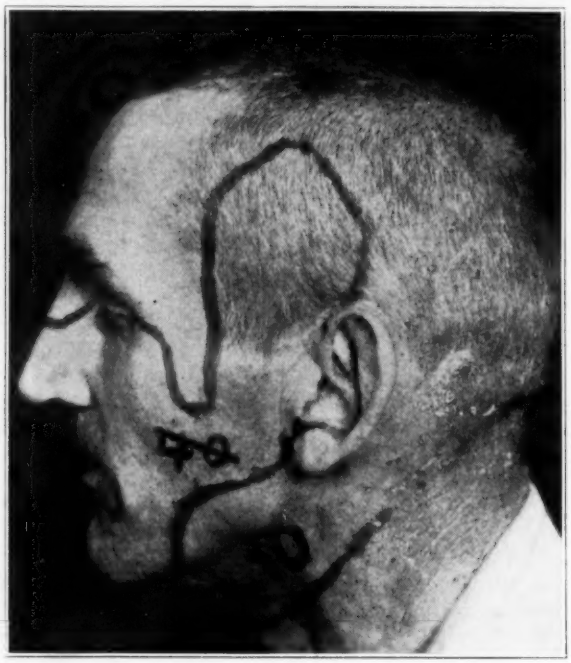

Fig. 3.—Photograph of a patient taken after tractotomy on the left side, showing analgesia in the area of the second and third trigeminal divisions, hypalgesia in the second and third cervical areas and preservation of sensitivity over the forehead.

the second and third cervical dermatomes was found as a rule when the third trigeminal division was involved.

The observations indicate that a subtotal transection of the intramedullary portion of the descending root of the fifth cranial nerve can be made, similar to the Spiller-Frazier subtotal section of the extramedullary portion of the sensory root of the fifth nerve. To preserve the first division, which is usually desired, the incision should begin 2 or 3, instead of 1 mm. dorsal to the last filament of the vagus nerve. If analgesia of the tongue and lips is essential, the tip of the knife must

be carried deeply and extensively enough that the superior medial tip of the crescent is included in the transection.

Surgical Problem.—The technical difficulties of the operation are few after thorough knowledge of the anatomic relations is obtained. The site for the section of the bulbospinal root is relatively superficial and easily exposed (fig. 5). The posterior inferior cerebellar artery is the only vessel which must be displaced, although this is not always necessary. The vagus nerve is the landmark for the section, and this structure need not be touched; neither is it wise to handle it. If the section of the root is done carefully and according to the specifications outlined by Sjöqvist, there is no need to fear serious complications.

Fig. 4.—Photograph of a patient taken aften tractotomy on the left side, showing complete analgesia of the forehead and hypalgesia of the cheek, chin and lips. The figures designate the pressure, expressed in grams, under which pinprick was felt as painful.

The advantages of section of the bulbospinal root of the fifth cranial nerve are as follows: 1. Pain and thermal sensations are abolished without loss of touch sensation. Because of this, patients are better able to chew their food without biting the tongue or lip. 2. Subjective numbness is absent, and because of its absence, postoperative paresthesias may be prevented. 3. In all instances the motor root is preserved. 4. The operative technic is not difficult. In contrast to the Dandy approach for section of the posterior root, the site of section is more

easily accessible, and the petrosal vein does not offer a constant source of trouble.

On the other hand, the disadvantages, as we see them, are: 1. In most instances there has been abolition of the corneal reflex. However, in our patients, as well as those whose cases have been reported in the literature, no ocular complications have developed. We appreciate that it is too soon after operation to make predictions regarding this complication. 2. In 3 of our patients the lip and/or tongue were not rendered insensitive to pain and temperature. It is questionable whether the pain of trigeminal neuralgia would have been relieved in these patients if the pain had had its origin in the lower lip or in the tongue. Failure to relieve pain in this region can be avoided by placing the transection correctly. 3. The transient complications which may arise from damage

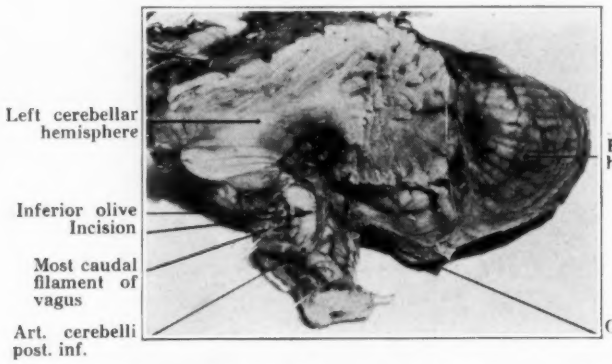

Fig. 5.—Specimen of the cerebellum and brain stem, in which the left cerebellar hemisphere has been partially removed at autopsy to show the location of transection of the descending root of the fifth cranial nerve.

of the restiform body, nucleus of Burdach, spinothalamic tract and recurrent laryngeal fibers of the vagus nerve offer no serious drawback to the operation. 4. From a technical standpoint, the operation is more difficult in patients with short, thick necks. 5. It has been stated in a discussion that patients subjected to this operation have a longer postoperative stay in the hospital. The average for our patients was ten days. This figure does not exceed appreciably the average for the temporal approach. 6. It is true that patients who have this operation do experience discomfort in the muscles of the neck for several months after the operation. This occurs in all patients who undergo a suboccipital craniectomy. However, many patients would gladly endure transitory discomfort of the neck for the guarantee that they will not suffer numbness of the face for the remainder of their lives.

SUMMARY

Experience with the section of the bulbospinal root of the fifth cranial nerve and the results obtained from patients subjected to this procedure permit the following conclusions:

1. The operation is practical from the technical standpoint. 2. Touch sensation of the face is preserved. 3. The subjective sensation of numbness is avoided. 4. The procedure is ideal for patients with malignant tumors of the face, since the exposure permits one to section the ninth cranial nerve as well as the upper cervical roots.

DISCUSSION

DR. FRANCIS C. GRANT, Philadelphia: Trigeminal neuralgia may render a patient uncomfortable but will never kill him. Therefore, when an operative procedure is proposed for the relief of trigeminal pain, the safest possible operative maneuver that is available should be selected. The transtemporal approach is a safe method. We have now 1,011 cases, with an operative mortality of 1.03 per cent. Since over 80 per cent of the patients were over 60 years of age, the mortality is relatively low. Therefore, when a change is contemplated in the operative approach for the relief of trigeminal neuralgia, consideration of the subject from every angle is required.

The complications that result from section of the fifth nerve through the temporal fossa are facial weakness, keratitis and paresthesia. Facial weakness and keratosis can, in the great majority of cases, be easily avoided.

In a recent review of a series of 925 patients operated on for trigeminal neuralgia, the records showed that 32 (3.4 per cent) complained of severe continuous burning paresthesia in the anesthetic area of the face. In these patients the intermittent paroxysmal tic pain had been eliminated, but the constant, intense paresthesia produced by the root section was more distressing than the original spasmodic pain. My own impression had been that this unfortunate complication was uncommon, and the figures were surprising and depressing. Furthermore, the more complete the anesthesia the more distressing and severe the paresthesia seemed. Whether the root was completely or partially sectioned made no difference in the appearance of the paresthesia.

When Sjöqvist published his monograph on medullary tractotomy, stating that pain sensation alone was abolished in the face without loss of touch and therefore without subjective sensory loss, a possible solution of the problem of postoperative paresthesias appeared.

Six cases of malignant disease of the face with intense pain in the trigeminal distribution were referred to us within a short time by Dr. Eugene Pendergrass, of the radiologic department. Since section of the sensory root of the fifth nerve was indicated for relief of pain, a tractotomy was done. I operated on 5 of the patients and Dr. Groff on the sixth. The results were extremely satisfactory. Pain was relieved without much loss of touch sensibility. Subjectively, the patient said the face seemed normal, without the dull, dead or swollen feeling of which the patients complain during the first days or weeks after root section. Three patients with true trigeminal neuralgia have also been operated on by this method, with equally encouraging results. The most noticeable postoperative complication has been a mild ataxia of the ipsilateral arm, which disappeared completely in two or three weeks.

The third case of trigeminal neuralgia was particularly interesting because the patient had most of her pain in the tongue. Sjöqvist has said that at times the pain in the third division may not be relieved by this operative procedure. However, she has been completely free from pain.

As far as the operative technic is concerned, it is much easier to expose the lateral aspect of the medulla where the incision is made than to expose the sensory root above and in front of the cerebellum where it emerges from the pons. No vessels are encountered except the posterior inferior cerebellar artery, which may be easily seen and avoided. To the neurosurgeon who has done many chordotomies the incision into the medulla presents no great difficulty. The problem is to discover accurately where and to what depth the incision should be made to assure complete section of all the pain fibers in the descending trigeminal root. That this technic is not difficult and that Sjöqvist's description and observations are accurate are shown by the results in our cases. Unilateral suboccipital craniectomy is easily carried out under local anesthesia. Curiously, when the tract is cut the patient will groan, but not sufficient pain is produced to cause struggling, as is the case when the root itself is cut under local anesthesia.

The operative approach to the medulla is as easy as that to the sensory root in the temporal fossa. If one can cut the tract with accuracy, assuring complete relief of pain, I believe that the subsequent lack of objective sensory changes in the face may go far toward eliminating paresthesias as a postoperative complication. I intend to give medullary tractotomy a further clinical test and have great hopes that it may supersede other methods of sectioning the trigeminal pain-conducting fibers.

Dr. William J. Mixter, Boston: It seems to me that this is an interesting and probably a valuable addition to the armamentarium in the treatment not only of trigeminal neuralgia but of cancer of the face and neck. I agree absolutely with what Dr. Grant has said in regard to the question of the paresthesias. The paresthesias are so distressing to some patients that one will often find a patient with perhaps a bit of the skin of his face scratched off after posterior root section. If this operation will eliminate the paresthesias, that accomplishment alone gives it a definite place in surgical therapy. The technic also has a real place in the treatment of the neuralgias involving primarily the first division (which of course are rare but which do occur), because the absence of postoperative corneal complications would make it advantageous to use this approach.

Dr. Grant has spoken of the fact that several of the patients were suffering from malignant disease. It seems to me that through this same incision it undoubtedly would be easy to approach the ninth nerve and the upper cervical nerves at the same time and thus completely to denervate the area most commonly implicated by the pain resulting from malignant disease occurring in the distribution of the trigeminal nerve.

Dr. Paul C. Bucy, Chicago: In the clinics of the University of Chicago Dr. Walker has performed this operation in 3 cases, no one of them a typical or straightforward example of trigeminal neuralgia. The first case was an instance of syringobulbia, with pain in the face, in which the results were entirely satisfactory. The second patient had been operated on five years previously for trigeminal neuralgia, with entirely satisfactory results but with the occurrence of trigeminal neuralgia on the opposite side of the face. Wanting to avoid giving this man complete anesthesia of the face, Dr. Walker performed this operation, and the results were satisfactory. The third patient was a woman with trigeminal neuralgia who, because of some outside contact with a patient who had been

operated on, was fearful of experiencing a facial palsy after the usual retrogasserian neurotomy. She also seemed to be an excellent candidate for the development of paresthesias. For that reason this operation was performed. The result in this case is the least satisfactory in the 3 cases. The pain has been materially reduced, but the patient states that it has not been abolished.

I agree absolutely with what Dr. Groff, Dr. Grant and Dr. Mixter have said regarding the advantages of this procedure. It seems to me that perhaps one may also hope that in such conditions as postherpetic neuralgia and syringobulbia it will be possible to obtain results with this procedure which are not to be obtained by retrogasserian neurotomy. On the other hand, one cannot overlook the fact that the operation has certain disadvantages. The anatomic landmarks are not clearcut and definite, and with that fact Dr. Grant agrees. Furthermore, the surgeon is perhaps less inclined to be radical in this operative procedure than he would be with the usual subtemporal retrogasserian neurotomy and for that reason may make an incomplete section of the spinal root of the fifth nerve.

Dr. R. A. Groff, Philadelphia: I wish to emphasize two points in connection with the procedure. The operation of sectioning the descending root of the fifth nerve in the medulla is still in an experimental stage. We are not over-enthusiastic about it. There are many parts of the procedure which need further study. At the present time it appears that patients with pain in the third division might not be relieved of pain, as was brought out by Dr. Bucy.

COLLOID CYSTS OF THE THIRD VENTRICLE

A REPORT OF FOUR CASES

M. R. SHAVER, M.D. (QUEEN'S)
TORONTO, CANADA

Colloid cysts of the third ventricle, once considered a rarity discovered only at autopsy, in patients dying suddenly and unexpectedly, are now diagnosed with a fair degree of assurance, and have been found to be amenable to suitable surgical treatment. Stookey,[1] in 1934, collected 34 cases from the literature, adding 3 of his own. Instances in which this tumor has been encountered have been reported with increasing frequency in recent years.

This report is based on examination in 4 cases in which colloid cysts of the third ventricle have been demonstrated. The patients showed similarity of symptoms, and all four cysts showed a rather marked uniformity in site of origin, size and gross and microscopic structure. Two of the cysts were removed successfully at operation, and 2 were recovered at autopsy in cases of sudden death.

All the cysts were observed hanging from the anterior portion of the roof of the third ventricle, and intimately associated with the choroid plexus in this region. They measured approximately 1 to 2 cm. in diameter and presented a rather smooth, thin, fibrous wall over which ran numbers of blood vessels. Villi of the choroid plexus were adherent in 2 cases. In each instance the only content was a greenish or grayish, translucent, gelatinous "colloid" substance, while microscopically the wall was lined on its inner surface with a characteristic columnar epithelium, which was ciliated in some cases.

Cysts showing similarity in many of these features have been described by various investigators, including Fulton and Bailey,[2] Byrom and Russell,[3] Zimmerman and German,[4] Rinder and Cannon,[5] Stookey,[1]

From the Departments of Surgery, Toronto General and Western Hospitals, and the Division of Neuropathology, University of Toronto.

1. Stookey, B.: Intermittent Obstruction of the Foramen of Monro by Neuroepithelial Cysts of the Third Ventricle, Bull. Neurol. Inst. New York **3**:446 (March) 1934.

2. Fulton, J. F., and Bailey, P.: Tumors in the Region of the Third Ventricle: Their Diagnosis and Relation to Pathological Sleep, J. Nerv. & Ment. Dis. **69**: 1 (Jan.); 145 (Feb.); 261 (March) 1929.

3. Byrom, F. B., and Russell, D. S.: Ependymal Cyst of the Third Ventricle, Lancet **2**:278 (Aug. 6) 1932.

(Footnotes continued on next page)

Dandy,[6] Masson,[7] Davidoff and Dyke[8] and Paterson and Leslie.[9] In these reports there is lack of unanimity of opinion as to the origin of the tumors, although the clinical manifestations and the structure of the cysts showed more uniformity.

REPORT OF CASES

CASE 1.—A woman aged 26 gave a history of recurrent attacks of headache associated with vomiting for two years. Her previous health had been good, and physical examination showed nothing abnormal aside from bilateral papilledema. A diagnosis of recurrent blockage of the interventricular foramen was made by Dr. W. A. Hawke. A ventriculogram showed large, dilated lateral ventricles with absence of air in the third ventricle, and a diagnosis of cystic tumor of the third ventricle was made.

At operation, performed by Dr. W. S. Keith, a right frontal bone flap was raised and the cortex just anterior to the motor area was incised. The lateral ventricle was observed to be dilated, and the interventricular foramen was obstructed by a grayish, smooth-walled cyst projecting from the third ventricle. The foramen was enlarged and the cyst removed, the patient making an uneventful recovery.

When seen four months after operation the patient was suffering from epileptiform seizures. Her attacks of headache had disappeared. A ketogenic diet and barbiturates were prescribed, and after this treatment the epileptiform attacks also ceased.

Pathologic Examination.—The cyst (fig. 1) was round and measured 1.5 cm. in diameter. The wall was thin and fibrous, with numbers of blood vessels scattered over its sides and upper surface. It contained thick, grayish green, translucent "colloid" material.

Microscopically, the wall was seen to be covered on its outer surface by flattened epithelial cells, similar to those covering the choroid villi. The outer part of the wall showed a tendency to separate spontaneously in some areas, and was composed of fibrous tissue and blood vessels. Several groups of small tubules lined with cuboidal epithelium were noted in different areas of this portion of the wall (fig. 2). This epithelium was not ciliated, and no blepharoplasts were noted.

On its inner surface the wall was lined with epithelium (fig. 3 *A* and *B*), which varied from one to several cells in thickness, the inner layer being columnar; the underlying layers were more flattened. Many of the columnar cells were

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4. Zimmerman, H. M., and German, W. J.: Colloid Tumor of the Third Ventricle, Arch. Neurol. & Psychiat. **30**:309 (Aug.) 1933.

5. Rinder, C. O., and Cannon, P. R.: Impaction of a Neuroepithelial Cyst in the Third Ventricle of the Brain, Arch. Neurol. & Psychiat. **30**:880 (Oct.) 1933.

6. Dandy, W. E.: Benign Tumours in the Third Ventricle of the Brain, Springfield, Ill., Charles C. Thomas, Publisher, 1933.

7. Masson, C. B.: Complete Removal of Two Tumors of the Third Ventricle with Recovery, Arch. Surg. **28**:527 (March) 1934.

8. Davidoff, L. M., and Dyke, C. M.: Congenital Tumours of the Rostral Portion of the Third Ventricle, Bull. Neurol. Inst. New York **4**:221, 1935.

9. Paterson, J. E., and Leslie, M.: Colloid Cyst of the Third Ventricle of the Brain: Report of a Case Operated on with Recovery, Brit. M. J. **1**:920, 1935.

ciliated and characteristically had the appearance of goblet cells, containing large vacuoles near their free borders. Many of these cells contained a homogeneous substance similar in appearance and staining properties to the colloid material within the cyst. The general appearance was that of secretory epithelium. Desquamated

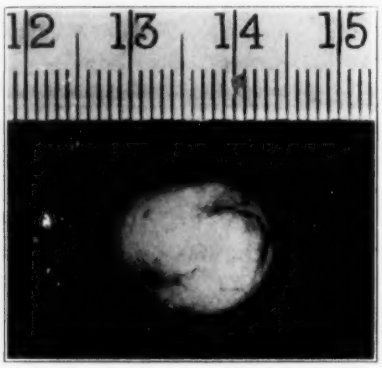

Fig. 1.—Cyst removed from the third ventricle in case 1, showing blood vessels on the surface of the wall.

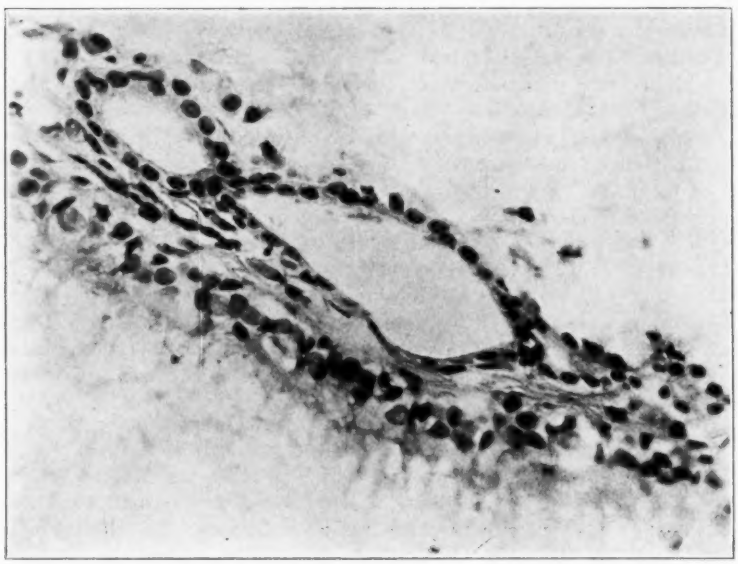

Fig. 2.—Area of the wall of the cyst in case 1, showing epithelium-lined tubules.

epithelial cells, with a somewhat similar but degenerated appearance, were observed embedded in the contents of the cyst.

The colloid was homogeneous, although crystals and cellular debris were present. Lymphocytes and large endothelial cells were scattered through the colloid, as

well as in small areas of the wall of the cyst, but the latter was not a marked feature. Mucin could not be demonstrated on staining with mucicarmine. Scarlet red showed the presence of lipoid free in the colloid, as well as within many

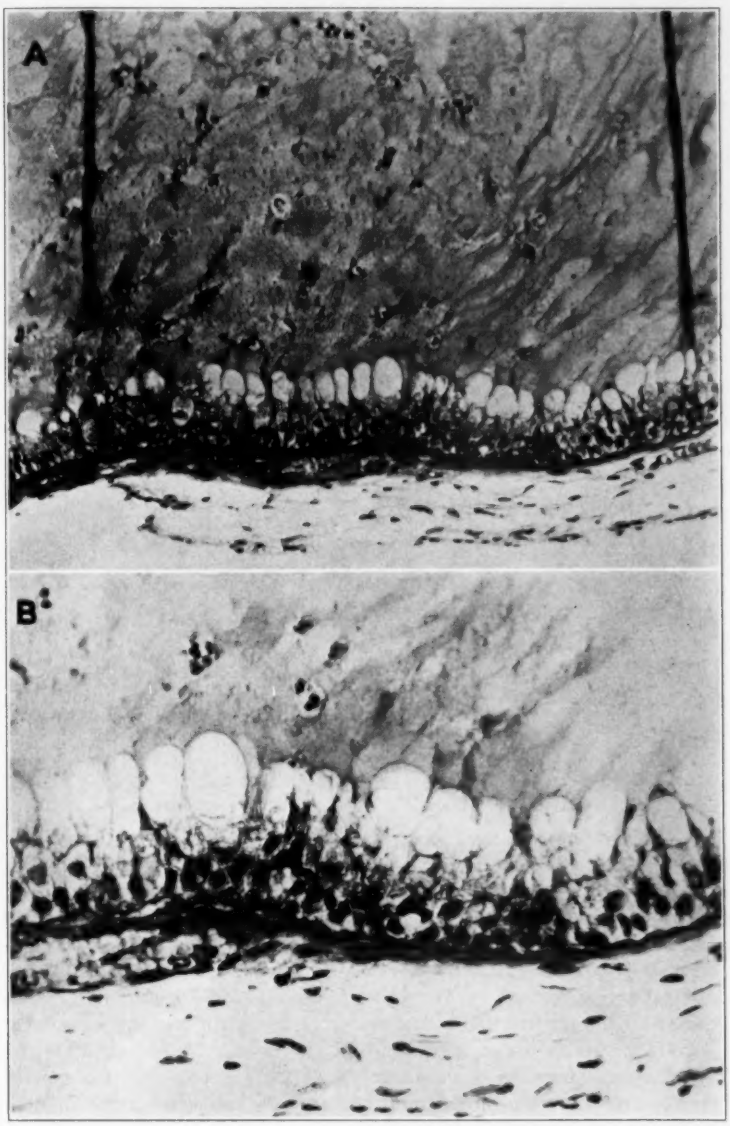

Fig. 3.—*A*, low magnification of the cyst wall in case 1, showing collagenous tissue with blood vessels and the surface covered by flattened choroid cells. Cellular debris may be seen in the colloid content. *B*, high magnification of the cyst wall seen in figure 2, showing an inner lining of epithelial cells, having the appearance of secretory epithelium, with goblet-shaped cells, containing vacuoles.

of the large endothelial cells. Fine deposits of similar material were observed in the tubules in the wall, and there appeared to be a fine distribution throughout the cytoplasm of the epithelial cells lining the cyst.

Case 2.—A woman aged 28 was admitted to the Toronto General Hospital, complaining only of progressive blurring of vision for five months. She had been in good health until she began to have periods in which she was unable to read or to see clearly. These attacks were of momentary duration. Examination of her eyes at this time revealed freedom from refractive errors, although there was papilledema on both sides. Examination failed to disclose any derangement of function of the heart and kidneys. The patient remained off duty until the time of her admission. Physical examination in the hospital disclosed only bilateral papilledema, which was somewhat more marked on the left side. Neurologic

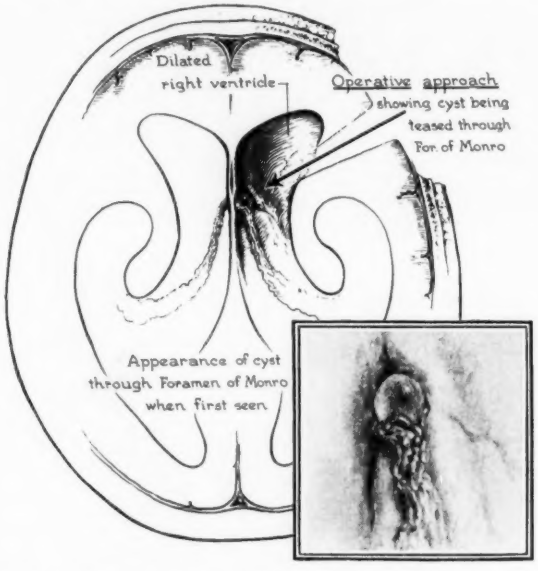

Fig. 4.—Diagrammatic illustration of the position of the cyst in relation to the operative approach. The inset shows the appearance of the cyst at operation.

examination gave normal results. A ventriculogram following the injection of 40 cc. of air showed distention of the right lateral ventricle with blockage of the corresponding interventricular foramen.

At operation, performed by Dr. K. G. McKenzie, the right lateral ventricle was entered by the transfrontal route, just anterior to the motor cortex (fig. 4). A cyst was found presenting at the foramen of Monro (fig. 5), and was excised after enlargement of the foramen upward and forward. The postoperative course was uneventful except for slight fever (102 F.). On subsequent examination the papilledema had completely disappeared, and there has been no recurrence of visual disturbance.

Pathologic Examination.— The cyst was similar to that described in case 1 (fig. 6). It measured 1 cm. in diameter and had a smooth, thin, fibrous wall which was traversed by blood vessels. The content was a greenish gray colloid material.

Microscopically, the lining epithelium closely resembled that of the first cyst in its secretory appearance, with vacuolated cytoplasm and goblet-shaped cells. The cells presented a brush border, but cilia and blepharoplasts could not be distinctly defined. Many of the cells were flattened and definitely did not possess cilia. The wall of the cyst showed little inflammatory invasion in this case. The outer

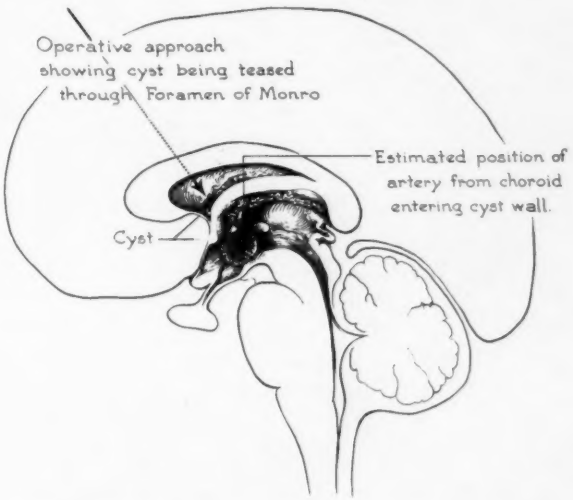

Fig. 5.—Diagrammatic illustration of the position of the cyst in case 2, as seen at operation.

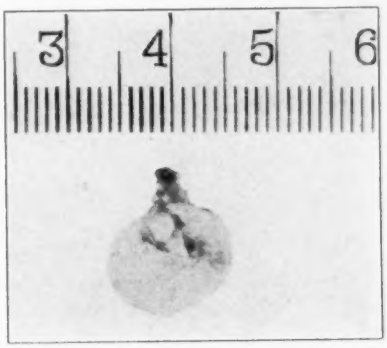

Fig. 6.—Cyst removed from the third ventricle in case 2, showing the pedicle and the point of rupture of the wall.

layer of the wall was vascular. The colloid content resembled that in the first case in staining properties and general appearance.

Case 3.—A girl aged 19 was said to have suffered from recurrent, severe attacks of headache for two months. These were described as being worse at night. Death occurred suddenly in one of these attacks.

At autopsy a small cyst was seen hanging from the roof of the third ventricle, with obstruction of the interventricular foramens and dilatation of the lateral ventricles. No other cause of death was observed.

Pathologic Examination.—The cyst measured 2 cm. in diameter, and in gross features was similar to the cysts already described. In addition, the dorsum presented adherent villi of the choroid plexus. The lining epithelium was ciliated (fig. 7) and several cells in thickness. The inner layer was composed of goblet cells, which presented the characteristic appearance observed in the first 2 cases. The outer fibrous layer of the wall showed a tendency to separate from the underlying portion, and inflammatory infiltration of the wall with lymphocytes, and polymorphonuclears and endothelial cells was a marked feature. Large numbers of these cells, showing degenerative changes, were embedded in the colloid. Sec-

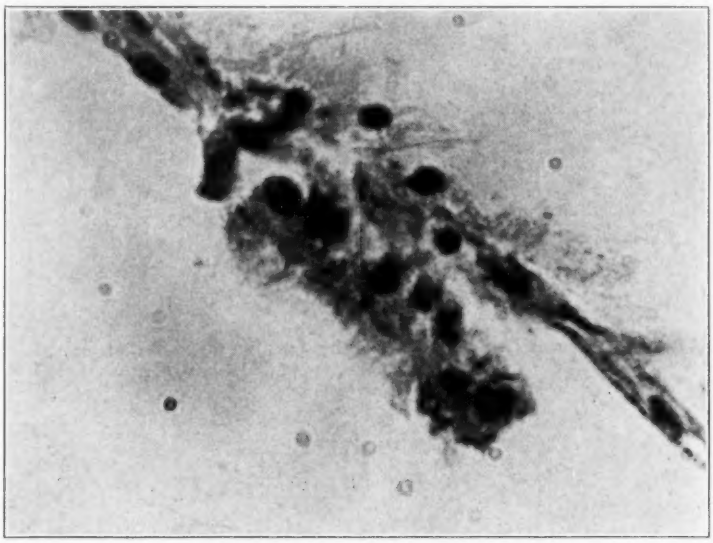

Fig. 7.—Epithelial lining of the cyst in case 3. The cells are ciliated, and the outer portion of the wall has separated.

tions of this cyst, stained with gold chloride–mercury bichloride (gold sublimate) and victoria blue, failed to exhibit glial tissue.

Case 4.—The patient was a young woman who died suddenly and unexpectedly after recurring attacks of headache for several months. At necropsy the only cause for death observed was a cyst similar in situation, size and gross features to that described in case 3.

Microscopically, this cyst contained colloid similar to that in the cases previously described, but the epithelium was more flattened and was absent in some areas; cilia and blepharoplasts could not be demonstrated. The cytoplasm had a granular appearance in sections stained with cresyl violet, the granules resembling the colloid in staining properties. Villi of the choroid plexus were adherent to the outer surface, while two rounded masses of cells, with small blood vessels in their central areas (fig. 8 *A*), were noted within the cyst. These masses of cells may represent a papillary projection from the wall of the cyst (fig. 8 *B*), although they were not covered by a well defined epithelial layer similar to that lining the cavity of the cyst.

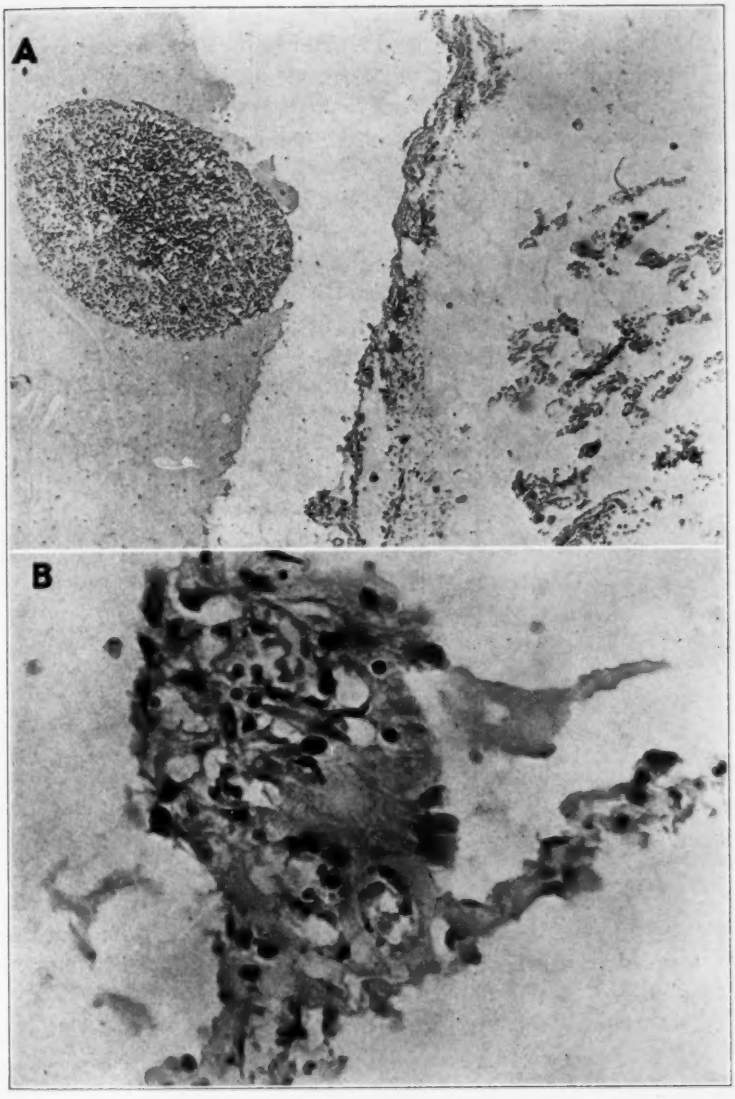

Fig. 8.—*A*, low magnification of the cyst wall in case 4, showing adherent villi of the choroid plexus, the epithelial lining and a round cellular mass, probably representing a papilliform projection. Inflammatory cells may be seen in both the wall and the contents of the cyst. *B*, high magnification of the cyst wall in case 4, showing small papilliferous projection and capillaries. There is no well defined epithelial lining, although a few cells similar to those lining the cyst appear.

COMMENT

Some cysts of the third ventricle undoubtedly result from degeneration in a glioma, while others may arise from epidermoid structures and parasitic infection. Other cysts, conforming more closely to those described in this series, appear to form a separate entity. These have been described as paraphysial cysts, colloid cysts, neuroepithelial cysts, choroid cysts and ependymal cysts, thus suggesting the obscurity of their origin.

Sjövall [10] first suggested a paraphysial origin in reporting a case in 1909, but the site of origin in a case reported by Stedman in 1883 has since been stated by Fulton and Bailey [2] to conform closely to the position of the paraphysis, which projects upward from the anterior portion of the roof of the third ventricle. Stookey [1] analyzed 37 cases, but in many of these he considered the cyst to have a lower attachment to the choroid plexus than would be likely with tumors derived from the paraphysis.

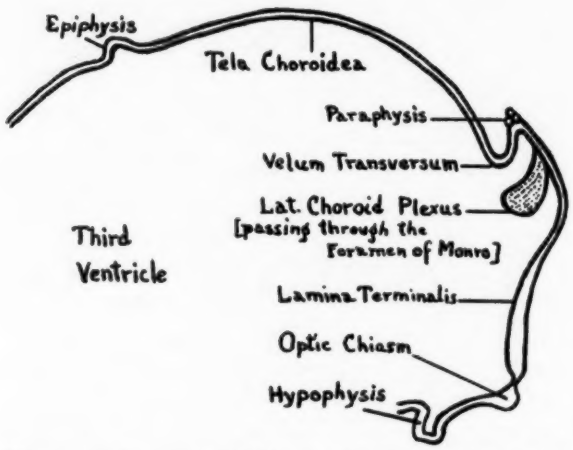

Fig. 9.—Diagrammatic representation of the paraphysis, in sagittal section, showing position and relation to other structures in the roof of the third ventricle.

The paraphysis was first described by Selenka [11] in 1891 as an embryonic structure arising from the roof of the third ventricle in lower vertebrates. This structure develops immediately cephalad to the velum transversum as a small midline diverticulum lined with fetal ependyma (fig. 9). From this, branch a number of tubules, forming an alveolar

10. Sjövall, E.: Ueber eine Ependymcyste embryonalen Charakters (Paraphyse ?) im dritten Hirnventrikel mit tödlichen Ausgang, Beitr. z. path. Anat. u. z. allg. Path. **47**:248, 1909.

11. Selenka, E.: Das Stirnorgan des Wirbelthiere, Biol. Centralbl. **10**:323, 1891.

arrangement and eventually becoming a complicated gland. The alveoli are lined by a single layer of columnar epithelium, with a network of thin-walled blood vessels in the intervening stroma, giving the appearance of a glandular secreting structure.

Other investigators, including Warren,[12] Minot,[13] Dendy,[14] Herrick,[15] Osborn [16] and Eycleshymer and Davis,[17] have since concluded that the paraphysis is a structure common to all vertebrates, at least in the embryonic stages. Francotte,[18] in 1894, identified the paraphysis in a human embryo of 12 weeks as a structure lying in the deeper portion of the falx, above and in front of the lamina terminalis. Bailey,[19] in 1916, discovered the paraphysial arch in the same position in a 19 mm. embryo, but did not find any evidence of glandular development. The choroid plexus of the lateral ventricles appeared to arise from its sides. Krabbe,[20] in 1936, failed to find any formation that could be regarded as a paraphysis in many of the mammalian embryos he examined, but noted the presence of a paraphysis in human embryos from 21 to 25.5 mm. in length. No similar structure could be seen in embryos from 4.1 to 17 mm. and from 29 to 50 mm. in length. He concluded that this phylogenetically old formation has probably disappeared in most other mammals, and is only a transitory structure in the human embryo, present at about the 75 day (20 mm.) stage.

In more recent articles on cysts in this region, McLean,[21] Trescher and Ford [22] and Zeitlin and Lichtenstein [23] have stated that they favored

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12. Warren, J.: The Development of the Paraphysis and Pineal Region in Mammalia, J. Comp. Neurol. **28**:75, 1917.

13. Minot, C. S.: On the Morphology of the Pineal Region Based upon Its Development in Acanthias, Am. J. Anat. **1**:81, 1901-1902.

14. Dendy, A.: On the Development of the Parietal Eye and Adjacent Organs in Sphenodon (Hatteria), Quart. J. Micr. Sc. **42**:111 (Feb.) 1899.

15. Herrick, C. L.: Topography and Histology of the Brain of Certain Reptiles, J. Comp. Neurol. **1**:37, 1891; **3**:77, 1893.

16. Osborn, H. F.: Contribution to the Internal Structure of the Amphibian Brain, J. Morphol. **2**:51, 1888.

17. Eycleshymer, A. S., and Davis, B. M.: The Early Development of the Paraphysis and Epiphysis in Amia, J. Comp. Neurol. **7**:45, 1897.

18. Francotte, P.: Note sur l'oeil pariétal de l'épiphysis, la paraphysis, et les plexus choroïdes du troisième ventricule, Bull. Acad. roy. d. sc. de Belgique **27**: 84, 1894.

19. Bailey, P.: Morphology of the Roof Plate of the Fore-Brain and the Lateral Choroid Plexuses in the Human Embryo, J. Comp. Neurol. **26**:79, 1916.

20. Krabbe, H. K.: Studies on the Existence of a Paraphysis in Mammalian Embryos, Brain **59**:483, 1936.

21. McLean, A. J.: Paraphysial Cysts, Arch. Neurol. & Psychiat. **36**:485 (Sept.) 1936.

22. Trescher, J. H., and Ford, F. R.: Colloid Cyst of the Third Ventricle, Arch. Neurol. & Psychiat. **37**:959 (April) 1937.

23. Zeitlin, H., and Lichtenstein, B.W.: Cystic Tumor of the Third Ventricle Containing Colloid Material, Arch. Neurol. & Psychiat. **38**:268 (Aug.) 1937.

such an origin, and Rehbock [24] suggested a developmental origin in this region; earlier writers accepted this explanation as possible, at least in some cases. As these tumors project from the roof of the third ventricle in front of the velum, their upward extension is limited by the pillars and bodies of the fornices. As they increase in size they sag down through the velum, to hang within the third ventricle between the foramens of Monro, carrying an outer covering composed of two layers of tela, lying back to back. Between these layers, as elsewhere in the choroid plexus, numerous blood vessels course on the dorsum and sides of the cyst.

Warren [12] has described small tubules evaginating from the roof of the diencephalon of the human embryo, immediately behind the velum transversum in the postvelar arch, from which the choroid plexus of the third ventricle develops. McLean suggested that these tubules may be similar histologically to the paraphysis. Pigment, which has been localized in the anterior portion of the velum in certain fish, and is absent more caudally, may form a possible means of differentiation.

Origin from structures farther back in the roof of the third ventricle is unlikely in view of their position and distinctive histologic structure.

Gardner and Turner [25] stated that they favored an origin from the choroid plexus and noted that these cysts bear an intimate relation to the choroid plexus, villi often being closely adherent to the surface and papilliferous processes being occasionally seen in the lining epithelium. They stated that the character of the lining epithelium indicates an origin in common with that covering the choroid plexus, as the latter is composed of ciliated cuboidal cells in the embryo, although the cilia are lost later.

Other authors have considered a possible origin from ependyma. Byrom and Russell [3] described a case in which they stated that the lining epithelium bore a close resemblance to ependyma.

Fulton and Bailey [2] preferred to designate these tumors as neuroepithelial cysts because of the uncertainty of their origin and the indefinite character implied in the name "colloid cyst."

The contents of the cysts are somewhat variable in physical and chemical properties. They have been described as containing yellow, brown or green gelatinous material, the physiochemical nature of which is unknown, although it does not take mucin stains and is not an albumin. Zeitlin and Lichtenstein suggested that hormones may be present, a suggestion which is not surprising as the ependyma over the hypothalamic area of the third ventricle has been described as secreting

24. Rehbock, D. J.: Neuro-Epithelial Cyst of the Third Ventricle, Arch. Path. **21**:524 (April) 1936.

25. Gardner, W. J., and Turner, O. A.: Neuro-Epithelial Cyst of the Third Ventricle, Arch. Neurol. & Psychiat. **38**:1055 (Nov.) 1937.

material with such properties. McLean,[21] in 1 of his cases, described a lipochrome giving a prussian blue color after fixation in Zenker's solution and treatment with concentrated sulfuric acid. Globules of similar material were observed in the lining epithelium. A similar pigment was found in a case reported by Rinder and Cannon,[5] who also demonstrated its presence with scarlet red. Similar results were obtained with scarlet red in case 1 in this series, the only one in which sections were stained by this method.

The epithelium in many of the earlier cases reported was noted to be of ciliated columnar type, and blepharoplasts were described. More recently, many instances in which the epithelium was more flattened, with absence of cilia, have been noted. Typically, the cells resemble goblet cells, with a secretory appearance, and the cytoplasm contains vacuoles and granules. The epithelium may show variation, being from one to several cells in thickness, and in some cases the surface cells are seen to be shed into the adjacent colloid, in which they are embedded. The outer layer of the cyst wall, composed of fibrous tissue derived from the double layer of the tela, often shows a spontaneous tendency to separate, and blood vessels may be numerous in this tissue. The covering epithelium of flattened cells is similar to that observed elsewhere over the choroid plexus.

In some cases tubules lined with epithelium similar to that lining the large cyst, or more flattened, have been seen in the substance of the wall. Case 1 in this series is a good example and lends support to the theory of origin from a primitive tubular structure. Inflammatory cells are frequently observed scattered through the wall and colloid and are more marked where pressure and chronic inflammatory change are severe, as in cases 3 and 4 in this series, in which autopsy was performed. The absence of cilia in some cases has been attributed to the presence of an inflammatory process and to pressure of accumulated contents on the cyst wall.

The clinical features in cases of these cysts have been studied by many investigators, including Fulton and Bailey,[2] Zimmerman and German,[4] Dandy[6] and Stookey.[1] No predilection for either sex can be noted, although the patients in the present series were women. Symptoms are noted first usually between the ages of 20 and 50, beginning with recurrent headaches, which are generally more severe in the frontal region. In occasional cases headache has not been an initial, or even a prominent, symptom. The headaches are typically sudden in onset and may be relieved as suddenly. They may be associated with loss of consciousness, and are characteristically relieved or exaggerated by alteration in position. Papilledema is found in the majority of cases, while in half the cases vomiting is noted. All these symptoms are referable to intermittent obstruction of one or both foramens of Monro

produced by the cyst or, if the cyst is large, to blocking of the aqueduct of Sylvius, with resulting intermittent internal hydrocephalus. This obstruction is subject to variation, depending on the position of the patient's head. An additional factor in producing the internal hydrocephalus may be obstruction of the striate and lateral choroidal veins at their junction to form the vein of Galen, leading to increased production of cerebrospinal fluid in the obstructed ventricle. The increased intracranial pressure accompanying the obstructive internal hydrocephalus is responsible for the fairly uniform clinical finding of papilledema.

Other symptoms, referable to pressure on neighboring structures, such as the hypothalamus, are less common and usually depend on the cyst attaining a larger size than is commonly seen now. Symptoms such as tachycardia, hypersomnia, diabetes insipidus and glycosuria may result. Byrom and Russell [3] recorded a case in which the patient, previously diabetic, was treated when in coma but failed to respond to insulin therapy. At autopsy a cyst was observed in the third ventricle. Mental dulness has been noted in some cases, while vegetative disturbances are noted occasionally. Muscular weakness, paresthesias and spasticity of extrapyramidal origin have also been described. A typical feature in many instances is the absence of symptoms between attacks. The course usually varies from one month to two years in duration, terminating in a sudden fatal attack. Two cases, in which the illness extended over eight and eleven years, respectively, have been explained by the suggestion that the cyst may rupture occasionally, with expulsion of its contents.

Diagnosis may depend on the absence of air in the third ventricle, as shown by a ventriculogram. If obstruction is not complete the tumor may be outlined in the third ventricle.

In 1934 Stookey [1] found the operative mortality to be 33.3 per cent among 6 patients treated surgically. Since that time numerous reports of successful operative treatment have appeared, and the impression is growing that these tumors are readily accessible via the frontal route and can be readily removed through the foramen of Monro, the whole being accomplished in a single operation.

Postoperative epileptiform seizures have been reported, as in case 1 in this series, but usually these tend to disappear and the outlook for the patient is exceedingly good.

CONCLUSION

Cysts of the type described here may all be considered to be similar in symptomatology, position and histologic structure to the so-called colloid cysts of the third ventricle reported in the literature. Absence of cilia is not uncommon. The fact that the cysts have been observed

only in the third ventricle suggests their origin from some structure to be found only in that region. If they were simple cysts of the choroid plexus one would expect to find them as frequently in other sites where the choroid plexus is present. Also, the commonly observed cysts of the choroid plexus, the result of cystic degeneration in the collagenous tela choroidea, have no lining epithelium and contain only thin albuminous fluid. The epithelium, which is present on the outer but not on the inner surface of the cyst, is similar to that covering the choroid plexus. It is not ciliated in man, except in the embryonic stage, and blepharoplasts are never seen.

While the lining epithelium of these cysts resembles ependyma in many respects, the type of secretion found in the cysts, together with their localization in this one position in the ependyma-lined cavities of the central nervous system, would indicate that they arise only from a specialized portion of ependyma.

SUMMARY

1. The most reasonable explanation of the origin of these cysts is that they arise from the paraphysis, which is an embryonic structure derived from the fetal ependyma of the anterior portion of the roof of the third ventricle. The histologic structure of the cysts seems to substantiate this view, as tubules are frequently observed in their walls and suggest origin from a glandular structure.

2. The symptoms are usually suggestive and when combined with evidence of blockage of one or both foramens of Monro, as shown in a ventriculogram, and with other neurologic findings indicating increased intracranial pressure and pressure on adjacent parts, make possible a preoperative diagnosis with a fair degree of certainty.

3. Surgical treatment of these cysts is remarkably successful. Both patients in this series who underwent operation recovered, with cessation of all symptoms referable to the tumor.

Dr. K. G. McKenzie, Dr. W. S. Keith and Dr. W. A. Hawke gave permission to report cases 1 and 2, and Prof. E. A. Linell made autopsy specimens available and gave valuable assistance in the preparation of this paper.

MYOCLONUS EPILEPSY

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Myoclonus epilepsy is a rare, but well recognized, clinical entity characterized by the occurrence of rapid, abrupt, irregular, jerky, involuntary contractions in one or several muscle groups, associated with generalized convulsions. Those afflicted with the disorder usually give a familial history of it or of essential epilepsy or of some other degenerative disease of the central nervous system. Several clinical entities characterized by the presence of myoclonic movements have been described, such as paramyoclonus multiplex of Friedreich,[1] intermittent myoclonia of Lundborg,[2] partial continuous myoclonia of Kozhevnikoff [3] and progressive familial myoclonia of Unverricht.[4] As in the case of many other degenerative diseases of the central nervous system, the forms mentioned are possibly variants of the same condition, some with and others without a hereditary or familial history. In addition to descriptions of the more common familial and hereditary forms, the literature contains reports of cases in some of which the disorder is said to have followed encephalitis, and in others psychic trauma. The pathologic basis of myoclonus epilepsy consists of degenerative changes in the central nervous system characterized mainly, though not uniformly, by the presence of inclusion bodies in the nerve and glia cells.

In this communication we present the clinical histories in 3 cases of the disorder, in 1 of which we had the opportunity to study the brain and spinal cord histologically.

From the Neurological Division and the Neuropathological Laboratory, the Montefiore Hospital.

Read at the Sixty-Fifth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 6, 1939.

1. Friedreich, N.: Neuropathologische Beobachtungen; Paramyoclonus multiplex, Virchows Arch. f. path. Anat. **86**:421, 1881.

2. Lundborg, H.: Der Erbgang der progressiven Myoklonusepilepsie, Ztschr. f. d. ges. Neurol. u. Psychiat. **9**:353, 1912.

3. Kozhevnikoff, A. I.: Besondere Form von kortikaler Epilepsie, Med. obozr. **38**:97, 1894; cited by Lafora and Glück.[16]

4. Unverricht, H.: Die Myoclonie, Berlin, Franz Deuticke, 1891; Ueber familiäre Myoclonie, Deutsche Ztschr. f. Nervenh. **7**:32, 1895.

REPORT OF CASES

CASE 1.—V. D., a married woman aged 23, born in the United States of Italian parentage, was admitted to the Montefiore Hospital on Jan. 2, 1936, complaining of jerky movements in various parts of the body and generalized convulsions with loss of consciousness, of six years' duration, and difficulty in gait and speech for the past two or three years. There was no family history of nervous or mental disease. There was no consanguinity. The patient's developmental history was normal. She was married at the age of 17 and had two pregnancies. From the first pregnancy there was a normal child, now 6 years of age, and the second was terminated by a therapeutic abortion four years ago, on account of the patient's illness. Except for an alleged uneventful attack of influenza in 1918, the medical history was without significance.

At the age of 17 the patient had a generalized convulsion while on her way to work. Although unmarried, she found herself four months pregnant; she became nervous and restless, frequently dropping things from her hands. The father of the child then married her, and five months later she gave normal birth to a normal child. Seven months later there suddenly appeared rapid, jerky movements in various groups of muscles in the extremities. These lasted a few minutes, after which she would shriek and fall down in a generalized convulsion. During the seizure she would lose consciousness for three or four minutes. On regaining consciousness she usually had severe headache and remained in bed for a day or two. The seizures occurred from two or three times a week to once every few months, but the jerky muscular movements, varying in intensity, were present almost continuously while she was awake. Gradually there appeared difficulty in speaking, and during the past year she began to fail mentally.

Physical Examination.—The essential findings were: eccentrically situated pupils, reacting sluggishly to light; myoclonic movements of the muscles of the eyes, face, tongue and extremities, the movements being more frequent and more marked during excitement than during rest; general bradykinesia, with diminished associated movements of the arms in walking; slight rigidity with a cogwheel phenomenon in the extremities; depressed tendon reflexes in the arms; tendency to motor perseveration; mild cataleptoid attitude; monotonous, dysarthric speech; clumsiness on performing skilled acts.

Mental Examination.—The patient appeared dull and retarded. There were difficulty in thinking and comprehending, poor cooperation, superficial play of feeling with swings from mild irritability to foolish smiling and definite evidence of a moderately advanced memory defect. A modified Stanford-Binet test showed the mental age to be not higher than 6 years. She had graduated from grade school, the age at graduation being unknown, and worked efficiently as a dressmaker up to the onset of the present illness.

Laboratory Data.—Examination of the blood disclosed 78 per cent hemoglobin, 4,000,000 red cells, 9,800 white cells and a normal differential count. The Wassermann reaction of the blood was negative. Blood chemical determinations showed 95 mg. of sugar, 10 mg. of urea nitrogen, 4 mg. of serum albumin and 2.26 mg. of globulin per hundred cubic centimeters. Results of a sugar tolerance test were normal. The cerebrospinal fluid was clear, colorless and under normal pressure; there were no cells; the protein content was 15, 22 and 29 mg., respectively, on three occasions; the Pandy reaction was negative; the gum mastic curve was 0000000000; the serologic reactions were negative. The urine was normal. The electrocardiogram revealed a sinus rhythm. Basal metabolic rates on four

occasions were plus 25, plus 18, plus 16 and plus 9 per cent, respectively. The blood pressure was 120 systolic and 75 diastolic. Roentgen examination of the skull disclosed slight hyperostosis of the frontal region, thickening of the bones of the vault and a moderate amount of sclerosis of bone in the floor of the anterior fossa. Encephalographic examination (by the lumbar route), performed on Feb. 17, 1936, disclosed nothing abnormal; another, on Jan. 19, 1938, showed moderate diffuse dilatation of the entire ventricular system but no ventricular shift, the dilatation being most marked in the posterior horns of the lateral ventricles.

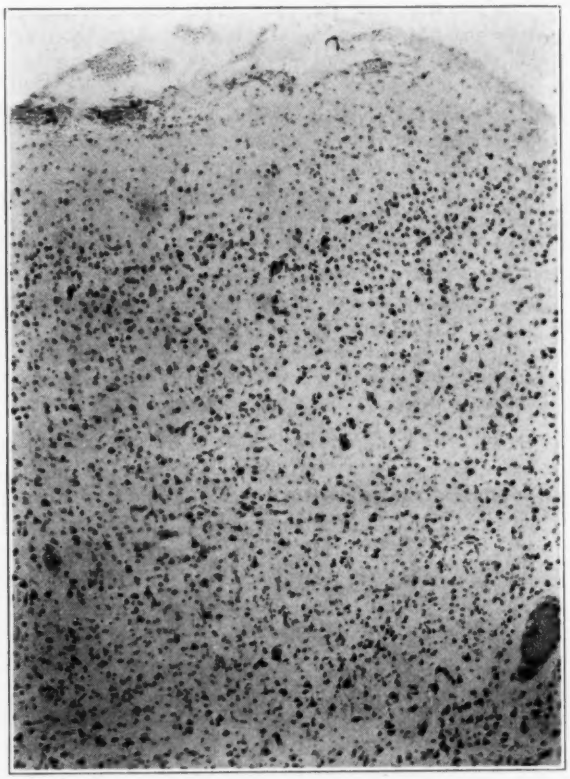

Fig. 1.—Distortion in the arrangement of the cytoarchitectural layers of the frontal cortex with dropping out of the nerve cells, especially in the upper three layers. Cresyl violet; × 40.

Course.—The generalized convulsions, varying in severity, occurred at irregular intervals in spite of large amounts of sedatives. The myoclonic movements persisted and became more severe and more frequent. At times extensor plantar responses of both big toes were elicited, and the abdominal reflexes were unobtainable. Mental deterioration became more marked, and there were periods during which the patient was entirely unresponsive. Toward the end of the illness there developed general flaccidity, marked generalized muscular wasting and stupor.

On Feb. 2, 1939 the patient refused to take nourishment, and examination of the chest disclosed signs of bronchopneumonia, to which she succumbed three days later.

Autopsy.—Macroscopic Examination: Brain: The pia-arachnoid had a glistening appearance and stripped readily. Otherwise, the brain and the vessels showed no abnormalities. The brain was cut coronally. Except for slight dilatation of the third and fourth ventricles, the ventricular system appeared normal in size.

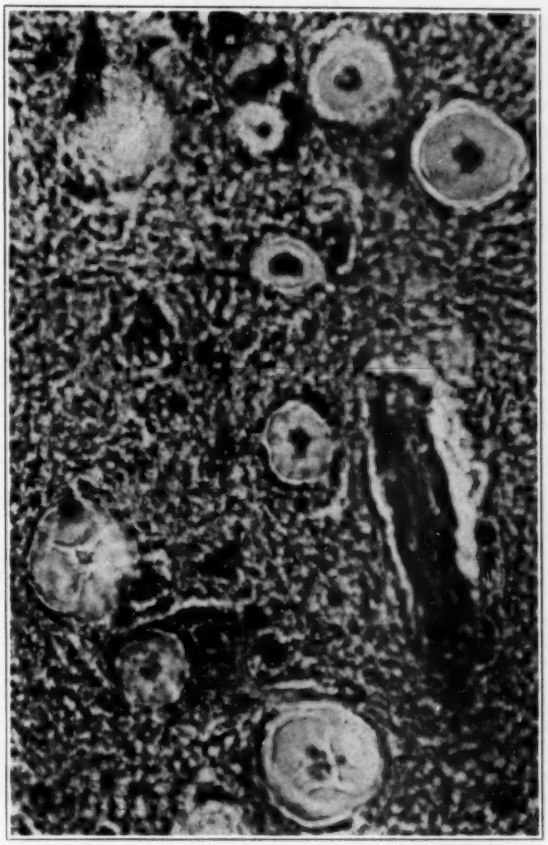

Fig. 2.—Homogeneous inclusion bodies in the nerve or glia cells, surrounded by an unstainable capsule separating it from the rest of the cell. The bulk of the inclusion body appears whitish, the central core dark. Azure carmine; × 480.

The white matter surrounding the dentate nucleus was grayish and seemed to be shrunken. The olivary nuclei stood out prominently.

Spinal cord: The spinal cord showed no gross abnormalities.

Microscopic Examination: Sections from various parts of the cortex, striatum, pallidum, thalamus, hypothalamus, substantia nigra, pons, cerebellum, dentate nucleus, medulla oblongata and spinal cord were stained by the myelin sheath

and cresyl violet methods. Sections from these regions were also stained by azure carmine, Best's stain, the Langhans modification of the iodine reaction, nile blue sulfate, sudan III, neutral red and the Holzer and Bielschowsky methods.

Cortex: In the frontal convolutions no abnormality was noted in the myelin sheath preparations. There were a few amyloid bodies in the meninges; these were irregular in shape and stained deeply; they were free and were not surrounded by cytoplasm or membrane. There was slight distortion in the arrangement of the cytoarchitectural layers (fig. 1), with occasional dropping out and pallor of the

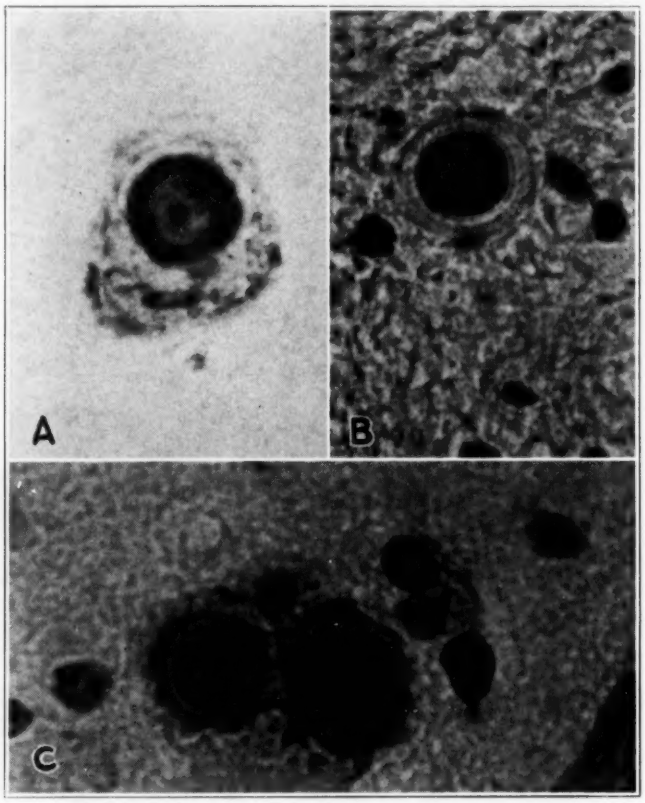

Fig. 3.—*A*, concentric form of inclusion body in a nerve cell, containing a small dark central core surrounded by several layers less deeply stained; × 400. *B*, concentric inclusion body enclosed in a glia cell, containing a large dark central portion and outer lamellae, staining lightly; × 900. *C*, three inclusion bodies in a nerve cell from the parietal cortex in amitotic division; × 900. Notice in two of these bodies a deep laminar zone at the periphery, separated by a light zone from the rest of the inclusion body. Cresyl violet.

nerve cells and prominence of the nuclei; this was most marked in the upper three layers. In the cresyl violet preparations, inclusion bodies, varying in size from 3 to 35 microns, usually round and taking a deep bluish stain, were present in the ganglion and glia cells; sometimes they replaced the entire cytoplasm

and nucleus of the nerve cell or of the glia cell. In general, two main types of inclusion bodies were seen: homogeneous and concentric. The homogeneous type stained uniformly and was surrounded by an unstainable capsule, separating it from the cytoplasm of the nerve or glia cell (figs. 2 and 7). In some inclusion bodies the core was formed by a more deeply stained portion in the form of an *x* or star (figs. 2 and 7). This was best brought out with the azure carmine stain, with which the bulk of the inclusion body appeared whitish or light blue and the core took a red or bluish stain. The homogeneous inclusion bodies were more prevalent in the glia cells (fig. 2). The concentric forms were observed both intracellularly and extracellularly and consisted of lamellae with an onion-like arrangement (fig. 3 *A* and *B*) and a central core or nucleus. The central nucleus appeared to consist of two parts, an inner, round, deeply stained and an outer, less deeply stained portion (fig. 3 *A*). Another concentric form consisted of a larger, deeply stained, homogeneous central part (fig. 3 *B*) and a pale outer zone formed by several lamellae arranged concentrically. In some instances the inclusion bodies in the nerve cells, although fairly large, displaced the nucleus and nucleolus to the periphery of the cell; in some of these cells the outlines of the nucleus and the nucleolus could be made out, whereas in others only the nucleolus could be seen. Some inclusion bodies were not much larger than the nucleolus, but they took a much deeper stain. Many of the nerve cells with inclusion bodies were completely deformed and showed various pathologic changes; in some the Nissl substance had completely disappeared, while in others part of it was preserved only at the periphery of the nerve cell. Occasional satellitosis and a slight increase in the microglia cells were noted. A small area of devastation was seen in the left second frontal convolution.

In the premotor and motor areas, the changes were similar to those in the frontal area. The few inclusion bodies noted were present in the large as well as in the small pyramidal cells. Occasional deposits of iron and calcium were seen in the white matter of the motor region.

In the parietal region, the arrangement of the cytoarchitectural layers was normal, but there were more inclusion bodies than in the motor and frontal regions. In one of the large cells there were several inclusion bodies (fig. 3 *C*). One nerve cell contained three such inclusion bodies; two of them had a dense laminar zone at the periphery, and was separated from the main portion of the corpuscle by a lighter zone (fig. 3 *C*). Two of these bodies were undergoing amitosis (fig. 3 *C*). Satellitosis and slight increase in the glia nuclei were also observed in this part of the cortex.

In the temporal, angular, supramarginal, lingual, hippocampal and occipital regions the arrangement of the cytoarchitectural layers was normal except for an occasional inclusion body. In the occipital region a few of the small and large pyramidal cells appeared washed out.

Diencephalon: In sections through the striatum a similar process was seen. Only a few nerve (fig. 4 *A*) and glia cells were involved. In most of these the inclusion bodies were oval or round and were surrounded by a fair amount of cytoplasm. Similar changes were observed in the thalamus (fig. 4 *B* and *C*), hypothalamus, corpus Luysi and red nucleus. In one area of the right external thalamic nucleus a few nerve cells were ballooned, resembling those seen in amaurotic family idiocy (fig. 4 *C*); they contained a large amount of pale cytoplasm and inclusion bodies which were smaller than those in other regions. These nerve cells, unlike those in amaurotic family idiocy, did not contain lipoid deposits. Throughout the diencephalic region some of the glia and nerve cells had inclusion bodies in the process of formation. Some of these bodies contained two nuclei

which were undergoing amitosis (fig. 5 *A, B, C* and *D*). Most of the inclusion bodies contained a homogeneous mass varying in size and surrounded by a lighter zone in which there were concentric lamellations or radiations (fig. 5 *C* and *D*).

Substantia Nigra: The substantia nigra appeared shrunken; its fibers stained poorly, and on the right side the nucleus was pale (fig. 6). Most of the nerve

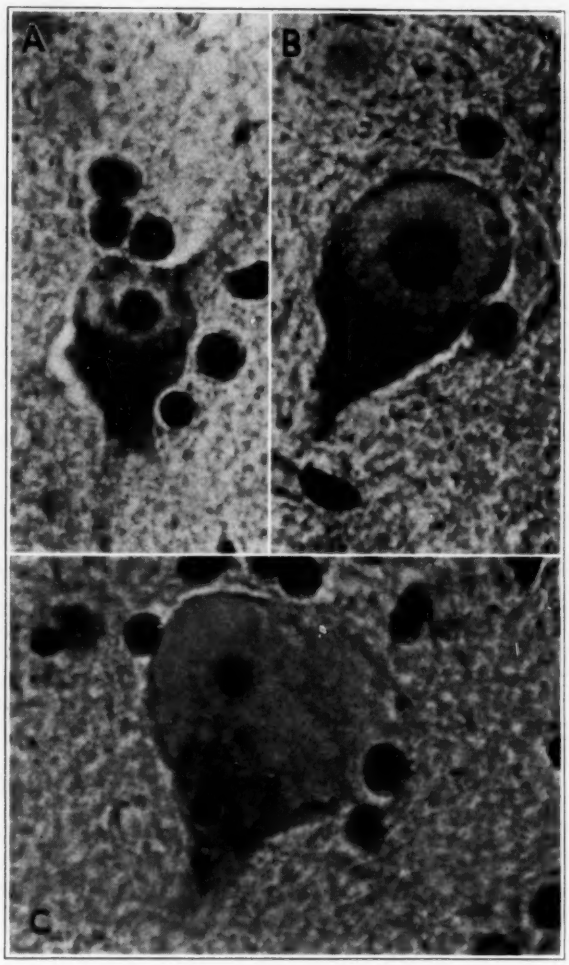

Fig. 4.—*A*, nerve cell of the striatum with inclusion body. The nucleus, which is barely perceptible is displaced to the periphery. *B*, nerve cell of the thalamus with inclusion body. The Nissl substance and the nucleus are displaced to the periphery. *C*, swollen cell, resembling those in amaurotic family idiocy cell, with inclusion body. Notice the loss in Nissl substance and the displacement of the nucleus to the periphery. Cresyl violet; × 900.

cells contained inclusion bodies, predominantly of the homogeneous type. In addition to the various forms already described, three or four or more such bodies

(fig. 7 *C*), varying in size and shape and with faceted surfaces (fig. 7 *A* and *B*), were present in some nerve cells. The nucleus of most of the nerve cells was displaced toward the axonal region (fig. 7 *A*, *B* and *C*), while the Nissl substance and iron pigment were displaced to the periphery (fig. 7 *C*). In some nerve cells the inclusion bodies were not larger than the nucleus (fig. 7 *C*) and were situated in the center of the cell. Occasional isolated inclusion bodies were also observed. The remaining ganglion cells had undergone various pathologic changes, some being completely destroyed. In some areas marked vacuolation of the ganglion cells of the substantia nigra was noted (fig. 7 *D*). The size of these vacuoles was somewhat similar to that of the inclusion bodies in the nerve cells (fig. 7 *D*). The iron pigment and Nissl substance of the vacuolated cells of the substantia nigra and

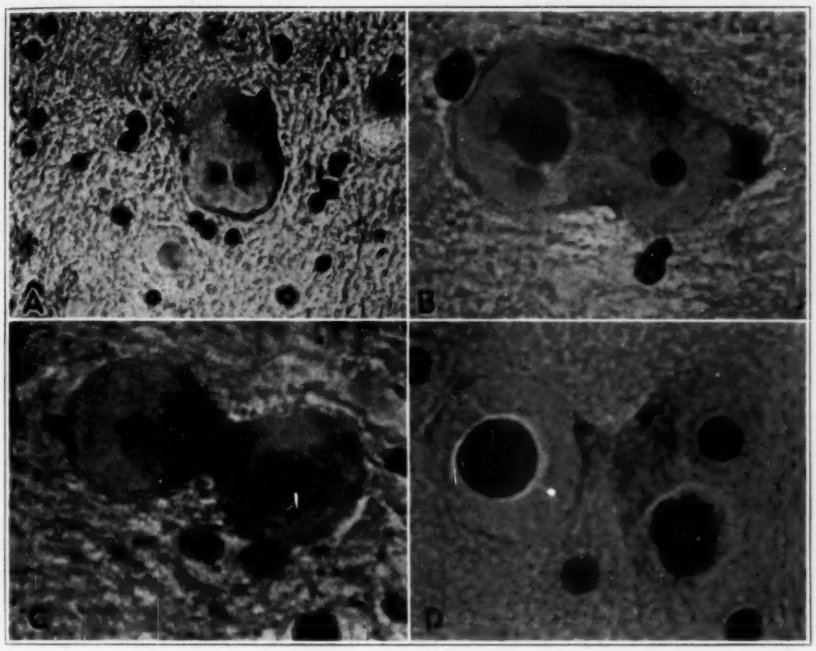

Fig. 5.—*A*, beginning inclusion body with two nuclei; × 480. *B*, two inclusion bodies in a nerve cell of the thalamus dividing by amitosis. Notice the displaced nucleus of the nerve cell and some preservation of the Nissl substance; × 900. *C*, two inclusion bodies in glia cells in amitosis; × 900. *D*, two inclusion bodies in amitosis which are almost completely separated; × 900. Cresyl violet.

of those with inclusion bodies were collected at the periphery (fig. 7 *A*, *B*, *C* and *D*). The glia nuclei and fibers appeared normal.

With the azure carmine stain, the inclusion bodies consisted of a central core which usually stained red, sometimes blue. The core was surrounded by a homogeneous or laminated structure which was either white or bluish (fig. 2). The remaining iron pigment of the nerve cells of the substantia nigra stained golden brown. The glia nuclei, with this stain, appeared red and the blood vessels and glia fibers blue. The red cells also stained blue. With the iodine reaction,

in accordance with Langhan's method, the inclusion bodies appeared bluish brown, indicating that the substance was probably amyloid. With the nile blue sulfate stain they had a bluish white tinge, the core and the surrounding cytoplasm appearing slightly bluish. Neutral fat with this method stains reddish blue, while fatty acids and other fatty substances stain from blue to violet. This method is not always reliable; therefore it is difficult to conclude that the substances of these inclusion bodies were not neutral fat, fatty acids or other fatty products. With neutral red the cytoplasm of the nerve cells stained reddish, while the inclusion bodies appeared whitish. This seems to indicate that they were not fatty acids. In sudan III preparations slight lipoid deposits were observed in the perivascular spaces (fig. 8). With this method inclusion bodies stained light blue and did

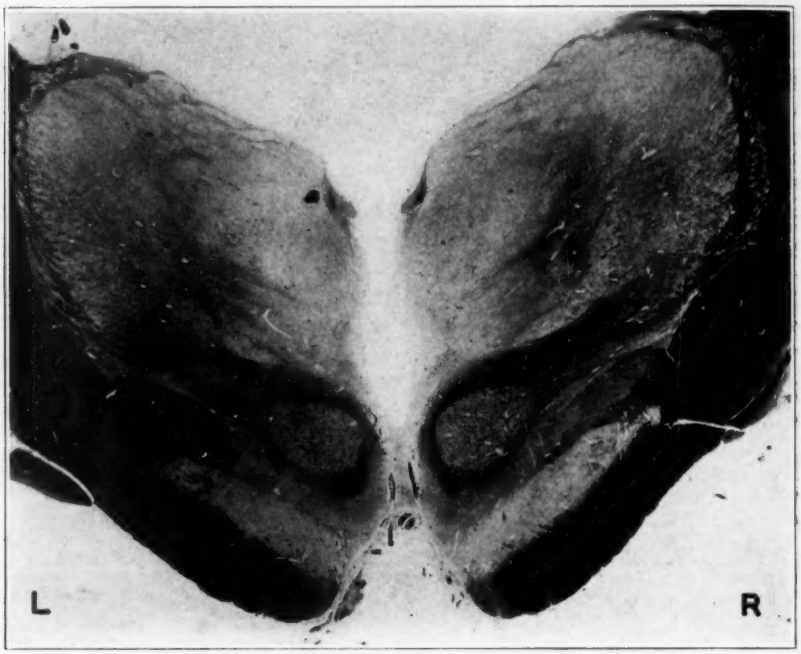

Fig. 6.—Coronal section through the region of third ventricle, showing bilateral shrinkage of the substantia nigra and slight pallor on the right side. Most of the inclusion bodies were observed in the substantia nigra and the dentate nucleus. Myelin sheath stain.

not appear to contain fatty deposits (fig. 8). Some of the nerve cells, especially in the hypothalamic region, were filled with fatty substances. In Bielschowsky preparations many of the nerve cells of the substantia nigra in the areas with inclusion bodies disclosed breaking down of the neurofibrillar network, with a tendency for the neurofibrils to collect at the perpihery of the cells, giving them somewhat the appearance of the fibrillary changes seen in Alzheimer's disease. With this stain the inclusion bodies usually appeared black or whitish (figs. 9 *A* and *B* and 11 *B*), while the nucleus stained poorly. Small collections of argentophilic substances were occasionally seen in the bodies (fig. 9 *B*). As has been

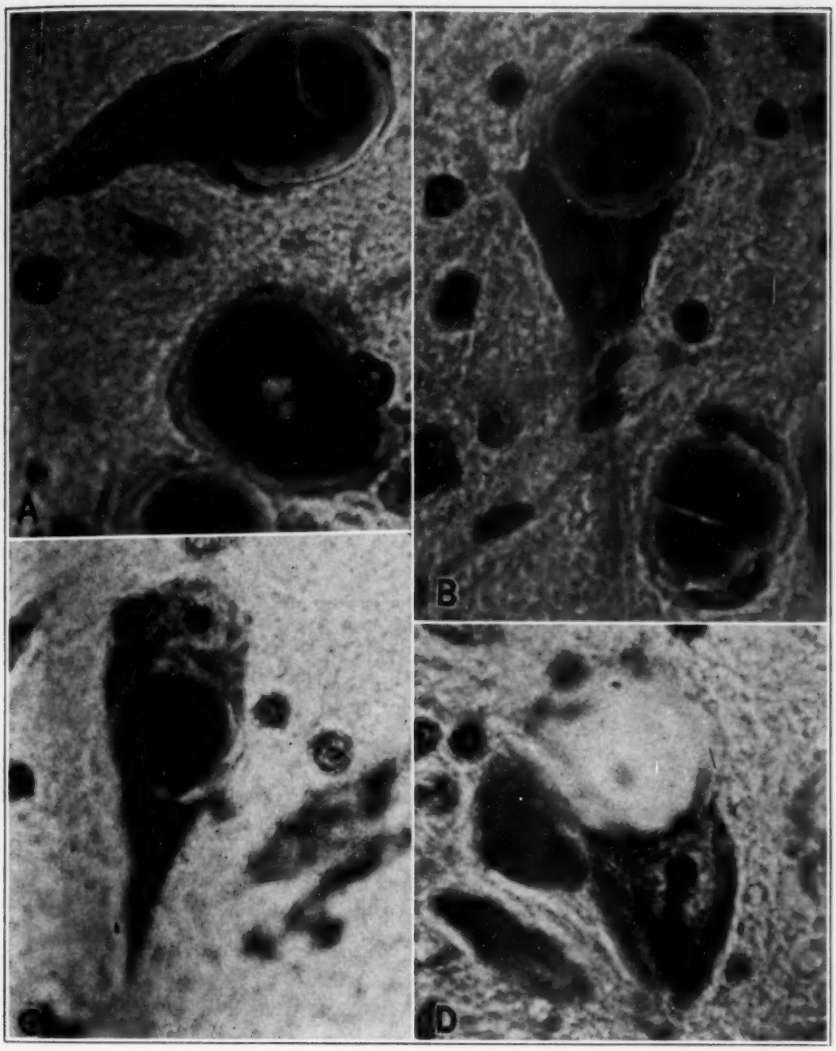

Fig. 7.—Varieties of inclusion bodies in nerve cells of the substantia nigra. Çresyl violet; × 900.

A and *B*, the several parts of the inclusion body are packed together with faceted surfaces; they contain a central core. Notice the displacement of the cytoplasm and nucleus toward the axonal region. *C*, nerve cell of the substantia nigra containing two types of inclusion bodies, one large and the other small. The Nissl substance and the iron pigment of the nerve cell are displaced to the periphery. *D*, vacuolated nerve cell of the substantia nigra. Notice that its size is that of the inclusion bodies seen in figs. *A*, *B* and *C*. The cytoplasm and nucleus are displaced to the periphery.

shown by Alexander,[5] neurofibrillar changes should be interpreted with caution, for they may be produced post mortem by soaking fresh human brain in certain fluids, such as distilled water and saline solutions. This "soaking change," according to Alexander, is always accompanied in the same tissue by argentophilia of the nuclei of the nerve and glia cells. The absence of fibrillary changes in the nerve cells of other parts of the central nervous system, except in the dentate nuclei, and of the argentophilia of the nuclei seems to indicate that the alterations in the nerve cells of the substantia nigra were specific, and most likely the result of displacement of the neurofibrillar network or of a disturbance in the chemistry of the cell. In Holzer preparations slight gliosis was noted, usually most marked in the region of the blood vessels; this, however, was not an outstanding process.

Fig. 8.—Fatty deposits in the perivascular spaces. The inclusion bodies stained poorly and did not show accumulations of lipoid. Sudan III; × 240.

Cerebellum: Occasional inclusion bodies were observed in the Purkinje cells and in the granular layer (fig. 10).

Dentate Nucleus: Next to the substantia nigra, the dentate nucleus was richest in inclusion bodies. They were, however, smaller than those in the substantia nigra (fig. 11 *A*). The cytoplasm of the nerve cell usually stained poorly and was almost completely devoid of Nissl substance, the inclusion bodies staining deep blue. Where the inclusion bodies were most numerous there was a slight increase in the glia nuclei. In Holzer preparations slight gliosis was noted, usually most marked in the region of the perivascular spaces; this, however, was not striking. In sudan III preparations lipoid deposits were seen in some of the nerve cells of the dentate

5. Alexander, L.: The Neurofibrils in Systemic Disease and in Supravital Experiments, Arch. Neurol. & Psychiat. **32**:933 (Nov.) 1934.

nucleus, but not in the inclusion bodies; the latter took a light bluish stain. In some areas lipoid deposits were also observed in the perivascular spaces. In Bielschowsky preparations the neurofibrillar network was destroyed, and the argentophilic substances were collected at the periphery of the nerve cell (fig. 11 *B*). The inclusion bodies stained homogeneously black (fig. 11 *B*). Basket and loops were also noted (fig. 11 *B*).

Pons: Sections through the superior part of the fourth ventricle, in myelin sheath preparations, showed no abnormalities. The central tegmental tract was

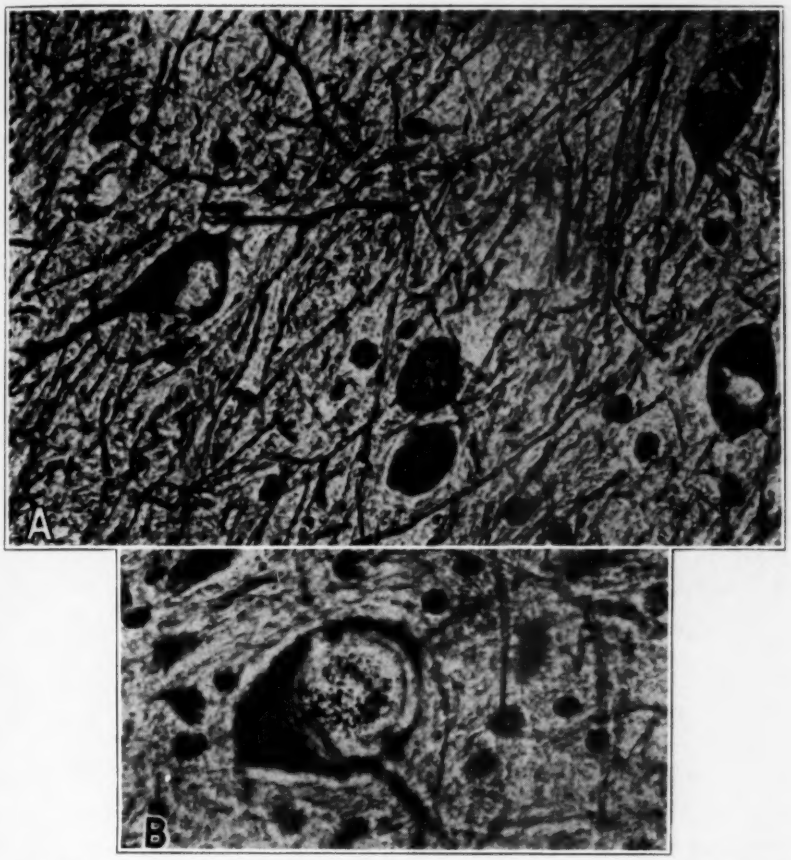

Fig. 9.—*A*, nerve cells of the substantia nigra showing collections of the neurofibrils at the periphery, giving them the appearance of fibrillary changes seen in Alzheimer's disease. The inclusion bodies appear whitish. × 480. *B*, inclusion body showing fine black granules in the center. The neurofibrillar network is displaced to the periphery. × 900. Bielschowsky stain.

normal. A few inclusion bodies and an occasional vacuolated nerve cell were observed in the locus caeruleus.

Medulla Oblongata: Sections through the medulla oblongata in the region of the nuclei of the sixth and seventh nerves disclosed no abnormalities in myelin sheath preparations. An occasional inclusion body was seen only in the superior olivary nucleus. In sections through the region of the nuclei of the tenth and twelfth nerves

the central tegmental tract appeared intact. The inferior olivary nuclei did not appear pseudohypertrophic. A few inclusion bodies were found in the region of the inferior olivary nuclei, mostly in the dorsolateral part or near the central tegmental tract. Occasional satellitosis and chronic changes in the nerve cells were noted in the paraolivary nucleus. Inclusion bodies were also seen in the vestibular nuclei, in large numbers in the nucleus dorsalis of the vagus nerve and occasionally in the nucleus of Roller. In sections through the crossing of the lemnisci, inclusion bodies were observed only in the inferior olivary nucleus.

Spinal Cord: No abnormality was noted in myelin sheath preparations. Helweg's tract appeared normal. Inclusion bodies were present neither in the anterior horn

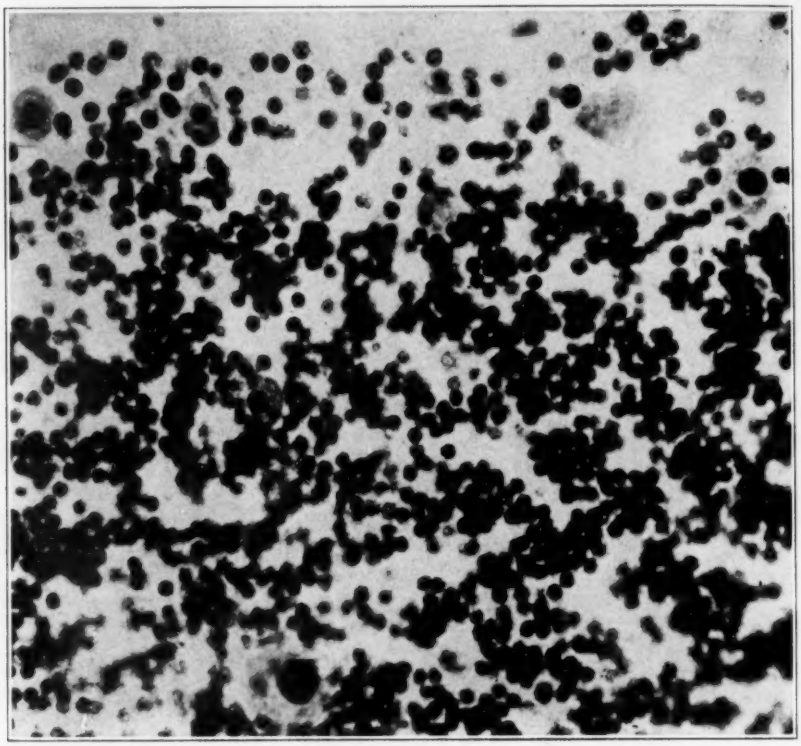

Fig. 10.—Inclusion bodies in the molecular (five) and granular layers (three) of the cerebellum. The inclusion bodies in the molecular layers are in the Purkinje cells; those in the granular layers are in the glia cells. Cresyl violet; × 480.

cells nor in any other cells of the gray matter. Some of the anterior horn cells, however, showed slight loss of Nissl substances. In Marchi preparations of the spinal cord, spinal nerve roots and peripheral nerves, no particular abnormality was noted; occasional breaking down and swelling of myelin were noted in Helweg's tract.

In this patient, the myoclonus was preceded by a few months by a generalized convulsion. Whether the pregnancy had any relation to the disease is difficult to state. Unlike the other cases of this disorder

reported, there was no family history of this or of other mental and nervous disease. Noteworthy clinical features, in addition to the myoclonus, were the mental and extrapyramidal symptoms.

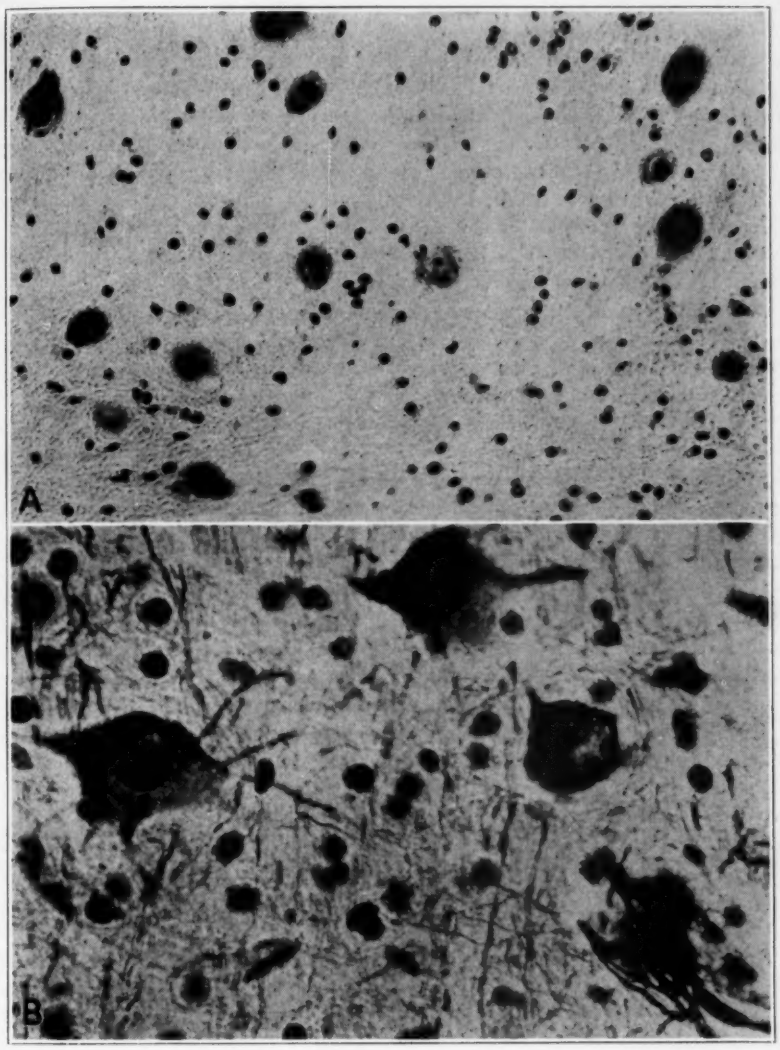

Fig. 11.—*A*, inclusion bodies in the nerve cells of the dentate nucleus. Cresyl violet; × 240. *B*, nerve cells of the dentate nucleus. Disintegration of the neurofibrillar network with collection of the argentophilic substance at the periphery of the nerve cells. Notice the basket cell. Some of the inclusion bodies in this structure stained homogeneously black. Bielschowsky stain; × 480.

Histopathologically, inclusion bodies were observed in the nerve and glia cells throughout the cortical convolutions, especially in the frontal

and parietal regions, and in other parts of the nervous system, such as the substantia nigra, dentate nucleus, inferior olivary complex, thalamic nuclei, vagus nuclei and cerebellum. The inclusion bodies were most numerous in the substantia nigra and dentate nucleus.

CASE 2.—H. T., a married man aged 46, was admitted to the Montefiore Hospital on Jan. 1, 1937, complaining of convulsions and "spasms" of about fifteen years' duration. He was born in Russia and had been in the United States for twenty-five years. He had not worked for the past ten years; prior to that he was a clothing factory operator. A 20 year old son was healthy; his wife had no other pregnancies. The patient had had bilateral otitis media in childhood. At the age of 17 he had a penile lesion, which was neither associated with nor followed by manifestations of syphilis. At the age of 27 he had an attack of influenza which ran an uneventful course. There had been no other illnesses. He had never been exposed to heavy metals and rarely drank alcoholic beverages.

The patient's father died at the age of 44 of apoplexy; his mother was living and well. There was no consanguinity. In one of his mother's sisters a condition resembling that of the patient appeared at the age of 50. A second cousin on the mother's side suffered from convulsions. A third cousin of the mother had a condition similar to that of the patient, which began at the age of 22 and to which he succumbed at 43. A brother died at the age of 26 in an institution for the feeble-minded, where he is said to have had a disease "resembling multiple sclerosis with myoclonus and ataxia"; he had no convulsions; his mental age at 26 was 4 years and 4 months. A daughter of the patient's brother had a convulsion during a febrile illness in childhood.

At the age of 30 the patient began to have spasmodic jerkings, of lightning-like rapidity, in the upper extremities and in the muscles of the neck; these persisted for about three years, when they also appeared in the trunk and lower extremities, so that he sometimes fell and injured himself. On one occasion he fell and fractured the left zygoma; on other occasions he sustained various injuries to the limbs. Most of the time the muscle jerkings appeared spontaneously; at other times they were initiated by emotional upsets, sudden noises or exposure of the eyes to strong light. The frequency of occurrence of the jerkings varied; the patient had good days on which they occurred only a few times and bad days during which they followed each other in rapid succession, with short free intervals. There were no days during which he was entirely free from them. The movements ceased during sleep. During some attacks the eyelids closed and trembled; during others they remained open, the head was turned to the right and the right side of the body became rigid and also was turned to the right. During still other attacks there occurred facial grimacing with grunting respiration. On several occasions after the subsidence of an attack the face assumed a blank expression and the patient became cyanotic, although consciousness was not affected.

In January 1932, while in bed, the patient had a generalized convulsion lasting about ten minutes; he was unconscious for half an hour. For the next four or five hours he was very weak but free from jerkings. After this, however, the jerkings increased in frequency and severity. Three months after this episode he was admitted to another hospital, where encephalograms disclosed marked atrophy of the cerebral cortex, especially in the frontal region.

In spite of intensive treatment with sedatives, the condition became progressively worse. During the past few years there had appeared disturbances in speech, incoordination of all four extremities and a broad-based, ataxic gait.

Physical Examination.—The significant findings on admission were: myoclonic movements in the muscles of the face, neck, trunk and all four extremities; bilateral deafness due to disease of the middle ear; inconstant nystagmus in all directions; slight weakness of the left external rectus muscle; moderate sclerosis of the retinal vessels; slight central weakness on the right side of the face, elicited only on mimetic innervation; choreiform movements of the tongue; broad-based, ataxic gait, with dyssynergia of all four extremities; rigidity of the left lower limb with a tendency to the cogwheel phenomenon; suggestion of a rebound phenomenon in both upper extremities, and cerebellar speech.

Mental State.—The patient is said to have been "peculiar." He was unusually irritable, moody and boastful, and had a tendency to exaggerate situations in which he was involved. During the past ten years his grandiosity had become more intensified and his lying more marked. On several occasions he had delusions of persecution and of marital infidelity. He had visual and auditory hallucinations. At times he was euphoric and facetious, at other times, evasive in his answers and given to circumlocution. Generally he was slow in thought, speech and action. Memory was poor for recent and past events, and retention and recall were defective.

Laboratory Data.—Routine laboratory examination of the blood, urine and spinal fluid, as well as roentgen examination of the skull, chest and vertebral column, disclosed no significant abnormality.

Course.—The patient's condition remained unchanged until November 1937, when he began to complain of gastrointestinal disturbances, which were attributed to external and internal hemorrhoids. In June 1938 he was subjected to hemorrhoidectomy under caudal anesthesia. After this procedure there developed cystitis, decubitus and cachexia. He died on July 18, 1938.

Permission for necropsy was not obtained.

Myoclonus was present in a maternal aunt, in two maternal cousins and possibly in a feebleminded brother. This is the only case in our group in which there was a definite familial history of the disorder. According to Lundborg,[2] the type described by Unverricht[4] is an inherited disease of a mendelian recessive order. The major epileptic attack in this case did not appear until twenty-four years after the onset of the myoclonus.

In this case, as in the first, there were symptoms referable to the cerebral hemispheres, basal ganglia and cerebellum. The atrophy of the cerebral cortex, especially the frontal region, as noted in the encephalogram, was probably the anatomic substratum for the mental deterioration in a person who was burdened with a preexisting psychopathic personality.

CASE 3.—J. R., a single woman aged 30, an accountant, was admitted to the Montefiore Hospital on Jan. 28, 1928, complaining of fear, crying spells and trembling of both shoulders. There was no history of a similar condition in the family. There was no consanguinity. The patient was said to have suffered from

otosclerosis for the past twenty-two years. About seven years ago she had "grip," with which she was in bed for three days and indisposed for about a week. Her menstrual history was normal.

On Dec. 3, 1927 she was knocked down by a horse and thrown over a 2 foot (60 cm.) railing on the sidewalk. She did not know whether she had struck her head; she was stunned for a while and sustained a bruise on her right leg. After this she became fearful; everything around her seemed "funny," and she complained of severe headaches which lasted about a week; they soon became milder but persisted on and off until admission. Owing to her fears and headaches she could not continue her work as efficiently as heretofore. One week after the accident she returned to work, but broke down and was sent home. She was then very irritable and had crying spells, which had become more frequent during the past month. Noises annoyed her greatly. She was restless and could not sleep. About three weeks later there appeared tremors of the right arm; these had become more frequent and more persistent. About a week before admission, tremor also appeared on the left side, but was less violent.

Examination.—There were: bilateral otosclerosis; myoclonic movements in both shoulder girdles, more marked on the right, and in the biceps and triceps muscles and the muscles of the forearm on the right side. In addition to the myoclonus, there were also involuntary movements during which the humerus rotated inwardly; they were increased by excitement. The muscles of the face, jaw and neck were not affected. Muscle tonus between movements was normal. There was a cogwheel phenomenon on the right side, with a suggestion of dystonic movement in the arm on that side. Otherwise neurologic examination gave normal results. Except for slight emotional instability with a tendency to depression, mental examination disclosed no abnormalities.

Laboratory Data.—The results of tests were normal.

Course.—The patient was given typhoid vaccine, after which the tremor was markedly diminished and the psychic condition much improved.

This case is of interest because the trauma, or the fright from it, was apparently the precipitating factor in the illness. There was no familial history of this or of other mental or nervous disorder. The myoclonus, in contrast to that in the first 2 cases, was not associated with grand mal seizures.

COMMENT

Nature of the Inclusion Bodies.—The precise chemical composition of the inclusion bodies has not as yet been ascertained. Histologically, most of them are analogous to amyloid bodies, or corpora amylacea. They are usually spherical, though, as in our case, they may vary in shape and size. They may be homogeneous or may consist of several concentric layers, which appear to increase in number with the age of the inclusion body. Marchand [6] expressed the belief that early in their formation the inculsion bodies are homogeneous and that the concentric

6. Marchand, L.: Degénérescence amyloïde de la cellule nerveuse, Ann. d'anat. path. **12**:1, 1935; Les myoclonies epileptiques, Encéphale **29**:217, 1934.

form is a later development. In either type there is a central core, varying in size and shape. In some instances they give a positive iodine reaction and take the Best stain for glycogen (Lafora's [7] and Westphal's [8] cases). Unlike glycogen, they are insoluble in water. They stain red, like other fatty acids, with neutral red. Because of these histochemical reactions, Spielmeyer [9] expressed the belief that possibly they are mixtures of sphingomyelin, phrenosin and a glycogen or carbohydrate body. In other instances they contain argentophilic substances. Histochemically, most inclusion bodies show the reaction between amyloid and hyalin; they differ, however, from the true corpora amylacea in their argentophilic contents.

The inclusion bodies may be either outside or inside the nerve or glia cells. They may not be larger than a nucleolus, their size usually varying between 3 and 35 microns. As they grow they displace the nucleus and nucleolus of the ganglion cell to the periphery of the axon, or they replace completely the contents of the nerve cell. When the nerve cell is completely destroyed they appear to lie free in the surrounding tissue. Some of the inclusion bodies may divide by amitosis. Occasionally several such bodies may be seen in one nerve cell.[9a] Secondary proliferative changes in the glia may be found. In some cases proliferation in the form of perivascular gliosis was observed in the cerebral cortex (Westphal and Sioli,[10] Volland [11] and Ostertag [12]). In our case, slight perivascular gliosis was observed in the substantia nigra and the dentate nucleus.

Amyloid bodies, phagocytosed by glia cells and analogous to inclusion bodies, may be seen in the brains of elderly persons. They are probably catabolic products associated with changes resembling those in senility. Cases of myoclonus epilepsy have been reported in which no inclusion

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7. Lafora, G. R.: Die Myoklonien und die Corpora amylacea in den Nervenzellen, Arch. de neurobiol. **4**:1, 1924; abstracted, Zentralbl. f. d. ges. Neurol. u. Psychiat. **37**:4, 1924.

8. Westphal, A.: Ueber eigenartige Einschlüsse in den Ganglienzellen (Corpora amylacea) bei einem Falle von Myoklonus-Epilepsie, Arch. f. Psychiat. **66**: 769, 1919.

9. Spielmeyer, A.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922.

9a. As far as we know, amitotic division of inclusion bodies has not been reported previously.

10. Westphal, A., and Sioli, F.: Weitere Mitteilung über den durch eigenartige Einschlüsse in den Ganglienzellen (Corpora amylacea) ausgezeichneten Fall von Myoklonusepilepsie, Arch. f. Psychiat. **62**:1, 1921.

11. Volland: Bericht über vier Fälle mit der Kombination Epilepsie-Paramyoclonus multiplex, Ztschr. f. d. ges. Neurol. u. Psychiat. **7**:180, 1911.

12. Ostertag, B.: Zur Histopathologie der Myoklonusepilepsie, Arch. f. Psychiat. **73**:633, 1925.

bodies were observed. Schultze [13] and Hunt [14] could find no pathologic changes in myoclonus epilepsy. Other observers described nonspecific changes in the pyramidal and other ganglion cells (Clark and Prout,[15] Volland [11]). The inclusion bodies in myoclonus epilepsy were first described by Lafora and Glück [16] in 1911, and later by Westphal and Sioli,[10] Pilotti,[17] Frigerio,[18] Bellavitis,[19] Schou,[20] Ostertag [12] and others. Because of the occurrence of inclusion bodies in other disorders, such as progressive mental deterioration with muscular atrophy (Spielmeyer [9]), double athetosis (Bielschowsky [21]), epidemic encephalitis, some postencephalitic conditions and paralysis agitans (Lewy [22]), observers have questioned whether they are pathognomonic of myoclonus epilepsy. Hodskins and Yakovlev [23] tabulated 18 cases of myoclonus epilepsy previously reported in the literature in which necropsy was performed between 1911 and 1928. In these cases various degenerative changes, and even softening, were observed. Characteristic in all, however, were the spherical inclusion bodies within the ganglion cells.

The presence of inclusion bodies in some of the virus diseases and the amitotic division of these bodies in our case suggest remotely that they may form the etiologic basis of this disorder. The process, in our opinion, however, seems to be essentially one of metabolic disturbance.

In addition to the inclusion bodies, some of the nerve cells of the substantia nigra and dentate nucleus in our case showed disintegration of the neurofibrillar network and collection of the argentophilic sub-

13. Schultze: Ueber Chorea, Poly- und Monoklonie, Neurol. Centralbl. **16**: 609, 1897.

14. Hunt, R.: Pathology of Paramyoclonus Multiplex, J. Nerv. & Ment. Dis. **30**:408, 1903.

15. Clark, L. P., and Prout, T. P.: Nature and Pathology of Myoclonus-Epilepsy, Am. J. Insan. **59**:185, 1902.

16. Lafora, G. R., and Glück, B.: Beitrag zur Histopathologie der Myoklonus-Epilepsie, Ztschr. f. d. ges. Neurol. u. Psychiat. **6**:1, 1911.

17. Pilotti, G.: Sulla mioclonie. Contributo clinica ed anatomo patologica, Policlinico (sez. med.) **28**:137, 1921.

18. Frigerio, A.: Su l'istopathologia della mioclonoepilessia, Note e riv. di psichiat. (pt. 3) **10**:319, 1922.

19. Bellavitis, C.: Contributo all' anatomia patol. della sindrome di Unverricht, Note e riv. di psichiat. **11**:459, 1923.

20. Schou, H. I.: Myoklonus-Epilepsie mit eigentümliche Gehirnveränderungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **95**:12, 1925.

21. Bielschowsky, M.: Beiträge zur Histopathologie der Ganglienzellen, J. f. Psychol. u. Neurol. **18**:513, 1912.

22. Lewy, F. H.: Zur pathologischen Anatomie der Paralysis agitans, Ztschr. f. Nervenh. **50**:50, 1914.

23. Hodskins, M. B., and Yakovlev, P. I.: Anatomo-Clinical Observations on Myoclonus in Epileptics and on Related Symptom Complexes, Am. J. Psychiat. **9**:827, 1930.

stances at the periphery of the nerve cells, approaching a process seen in Alzheimer's disease. Occasional baskets and twisted cords were also seen. Senile plaques, as observed in Alzheimer's disease, however, were not observed in our case. These alterations were considered by Alzheimer and others to be the result of catabolic changes in the argentophilic substance. As some of the inclusion bodies in a number of the reported cases contained argentophilic substances, it may be postulated that the inclusion bodies and the collection of the neurofibrillary network at the periphery of the nerve cells and its disintegration are parts of the same metabolic changes. As the nerve cells without inclusion bodies show no such changes, it is possible that the inclusion bodies may have compressed the neurofibrillar network, causing its displacement and disintegration.

Regional Distribution of Inclusion Bodies and Their Influence on the Production of Symptoms.—The inclusion bodies are apparently found predominantly in specific areas. Although in our case, as well as in some of the other cases reported, they were distributed throughout the central nervous system, they were most numerous in the substantia nigra and in the dentate nucleus. In Westphal and Sioli's case [10] they were most abundant in the thalamus, nucleus ruber and dentate nucleus. In other instances (Ostertag,[12] Bellavitis [19] and others) the greatest number were in the substantia nigra. The specific selection of certain areas may possibly account for the extrapyramidal and cerebellar symptoms and signs in cases of this disorder. In only a few cases were these bodies seen in the ganglion cells of the cerebral cortex. Although Friedreich [1] and Unverricht [4] claimed that the increased irritability of the anterior horn cells is the cause of the myoclonus, disease of these nerve cells has rarely been demonstrated by others, and none was found in our case.

The syndrome of rhythmic palatal myoclonus, in which the localization of the lesion has been accurately determined, may possibly be of aid in the understanding of myoclonus epilepsy. It is well established that in palatal myoclonus, as shown by several observers and by one of us (Davison and his associates [24]), the lesion may be situated in the central tegmental tract, the inferior olivary complex, the dentate nucleus and the tracts connecting these nuclei. In most cases of palatal myoclonus the central tegmental tract was involved. The frequency of involvement of the dentate nucleus in myoclonus epilepsy seems to indicate that myoclonic movements are possibly an expression of involvement of this structure. Lesions of the central tegmental tract in cases of myclonus epilepsy were not reported by other observers. In our case this tract

24. Davison, C.; Riley, H. A., and Brock, S.: Rhythmic Myoclonus of the Muscles of the Palate, Larynx and Other Regions, Bull. Neurol. Inst. New York **5**:94, 1936.

was intact, and inclusion bodies were not seen anywhere along its course, except near the olivary nuclei; the latter, however, did not have the pseudohypertrophic appearance seen in some cases of palatal myoclonus. The slight involvement of the central tegmental tract and of the inferior olivary nuclei in our case suggests that disease of these structures and of the dentate nucleus may also play a role in the production of myoclonic movements.

The generalized convulsions may be explained on the basis of cortical involvement. In our case Sommer's sector and the rest of the hippocampus appeared intact, except for a few inclusion bodies. In Ostertag's [12] case, however, there was sclerosis of the cornu ammonis, and, as is well known, disease of this structure was stated by some authors (Spielmeyer [9] and others) to be almost pathognomonic of the cause of epilepsy.

Many observers have stated that petit mal attacks and myoclonus epilepsy are opposite variants of grand mal attacks. This apparently has been demonstrated in electroencephalographic studies by Grinker and his associates.[25] Simultaneous leads from the occiput and the frontal region, according to these authors, seem to leave little doubt that the myoclonic attack is built up from the frontal region and radiates over the brain posteriorly before it culminates in a major seizure. The observers suggest that myoclonia is a homologue of continuous or intermittent prodromes sometimes evident, but often obscured, in other types of epilepsy.

The mental symptoms in our cases were possibly caused by the slight changes observed in the frontal and other convolutions. These consisted of slight distortion in the arrangement of the cytoarchitectural layers, dropping out of nerve cells, occasional small areas of devastation, the presence of a small number of inclusion bodies and slight glial proliferation.

The extrapyramidal symptoms were the result of the extensive involvement of the substantia nigra. Whether this structure was the cause of the myoclonic movements through its possible connection with the central tegmental system is difficult to state. It is of interest to recall that in parkinsonism with tremor the substantia nigra is invariably involved. Our 3 patients all showed extrapyramidal symptoms. Hodskins and Yakovlev [23] have stressed the extrapyramidal and cerebellar symptoms and expressed the belief that myoclonus epilepsy is an amyostatic syndrome because the extrapyramidal signs and the myoclonus readily appear when there is a change in posture. In case 2 there were choreiform movements of the tongue, which may have been caused by partial involvement of the striatum (caudate nucleus and putamen). A few inclusion bodies were seen in the striatum in case 1.

25. Grinker, R. R.; Serota, H., and Stein, S. I.: Myoclonic Epilepsy, Arch. Neurol. & Psychiat. **40**:968 (Nov.) 1938.

In our case in which necropsy was performed cerebellar symptoms were not recorded. This is readily explained by the presence of only a small number of inclusion bodies in the cerebellum and by the absence of other changes in this structure. In case 2, in which cerebellar signs appeared, the cerebellum may have been extensively involved.

The outstanding neurologic symptoms, in addition to the myoclonus, apparently depend on the region in which the pathologic process is most extensive. In cases in which there are marked extrapyramidal symptoms there are extensive lesions in the basal ganglia, especially in the substantia nigra. In cases in which there are pronounced cerebellar symptoms the cerebellum and dentate nuclei are the main sites of the inclusion bodies. In cases in which there are mental symptoms the frontal and other cortical convolutions should show pathologic changes.

CONCLUSION

Three cases of myoclonus epilepsy are reported. A familial history of the disorder was found only in case 2. In cases 1 and 2 the myoclonus was associated with mental symptoms and generalized convulsions. In addition to extrapyramidal symptoms and signs present in all 3 cases, cerebellar signs were noted in case 2.

In case 1 the central nervous system was studied histopathologically. Inclusion bodies, consisting of amyloid and argentophilic substances, with amitotic division in some, were observed throughout the nerve and glia cells of the central nervous system, except the spinal cord. The substantia nigra and the dentate nuclei were the main sites of these bodies. In correlating the clinical picture with the pathologic changes we are inclined to attribute the mental symptoms to involvement of the cerebral convolutions, especially the frontal, and the so-called extrapyramidal symptoms to lesions in the substantia nigra. The myoclonus may possibly be due to the changes in the dentate mechanism, as in palatal myoclonus.

DISCUSSION

DR. TRACY J. PUTNAM, New York: Detailed histories of cases presenting unusual features, especially when accompanied by reports of histologic examination of the brain, are of interest and value. The point which might arouse discussion is the authors' statement that myoclonus epilepsy is a rare condition. The definition which they give would seem to include simple muscular "shocks," and these are far from rare in patients with epilepsy.

Muskens devoted a large part of his book on epilepsy to myoclonus, which he considered the basic reflex action of epilepsy. Of 400 patients whom he questioned, 60 per cent gave a history of myoclonic shocks. In experiments with animals he found that lesions of the pyramidal tracts impeded the occurrence of myoclonic reflexes. He stated the belief that the center of reflexes lay in the pons and the medulla and that tactile and acoustic stimulation could accentuate them.

One might reasonably suppose that, like other manifestations of epilepsy, myoclonic phenomena might vary in severity, in the number and distribution of muscles involved and in the pathology. Simple myoclonic shocks may be merely manifestations of petit mal with an unusual prominence of muscular twitching, which is almost invariably discernible in petit mal, and with an unusual prominence of the spike in the electroencephalogram.

One such case was illustrated by an electroencephalographic record made by Dr. Gibbs. The patient's violent muscular jerks, which involved the arm and the muscles of the upper part of the trunk, were synchronous with the high spike of the three, a second wave and spike formation. Evidences of petit mal are usually most prominent over the frontal areas. In this case the pattern was most clearly marked in the left frontal area. This patient's attacks, though petit mal, were reduced about one half in number by the use of dilantin (sodium diphenyl hydantoinate). In other patients, movements which were more choreiform were not accompanied by cortical electrical changes. Presumably in these patients the disturbance was confined to subcortical areas.

More pathologic observations in these cases are greatly needed. The demonstration of inclusion bodies in 1 case is of much interest, though the fact that similar bodies have been demonstrated in cases of senility and other conditions suggests that the pathologic picture is not exclusive for this type of epilepsy.

Dr. Stanley Cobb, Boston: This condition is remarkably interesting. I wish to ask if the author would be willing to express an opinion as to the etiologic factors. Is the condition perhaps a virus disease?

Dr. Charles Davison, New York: I really am unable to express a definite opinion. Inclusion bodies are found in patients with virus diseases. At present there is not sufficient evidence to explain the cause of this disease. From the pathologic and chemical studies of these bodies it would appear that one is dealing with some metabolic disturbance. I would, however, withhold any opinion as to the etiologic character of the disorder.

ELECTRICAL ACTIVITY OF THE EXPOSED HUMAN BRAIN

DESCRIPTION OF TECHNIC AND REPORT OF OBSERVATIONS

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AND
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ST. LOUIS

The application of electrical methods to the study of cerebral function is still in an experimental stage. In 1923 Grant,[1] using a simple Wheatstone bridge arrangement, reported marked diminution in the electrical resistance of tumor tissue as compared with that of normal brain. Berger[2] amplified electric potentials set up in the brain and ascribed changes in potential to nervous activity. Foerster and Altenburger[3] succeeded in recording characteristic changes in potential in several cases of tumor of the brain. Subsequently, electroencephalographic methods have resulted in the accumulation of a considerable amount of data, especially with respect to the epileptic syndromes.[4] Recently, important

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* Visiting Fellow of the Rockefeller Foundation, 1937-1938.

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From the Neurosurgical Services of the Barnes and St. Louis Children's Hospitals, and the Washington University School of Medicine.

This work has been aided by a grant from Child Neurology Research and the John and Mary R. Markle Foundation; the cost of the apparatus for the most part was defrayed by a grant from the Ella Sachs Plotz Foundation.

1. Grant, F. C.: Localization of Brain Tumors by Determination of the Electrical Resistance of the Growth, J. A. M. A. **81**:2169-2171 (Dec. 29) 1923.

2. Berger, H.: Ueber das Elektrenkephalogramm des Menschen, Arch. f. Psychiat. **87**:527-570, 1929; **94**:16-60, 1931; **97**:6-26, 1932; **98**:231-254, 1933; **99**:555-574, 1933; **100**:301-320, 1933; **101**:452-469, 1933; **102**:538-557, 1934; **103**:444-454, 1935; **104**:678-689, 1936.

3. Foerster, O., and Altenburger, H.: Elektrobiologische Vorgänge an der menschlichen Hirnrinde, Deutsche Ztschr. f. Nervenh. **135**:277-288, 1935.

4. Gibbs, F. A.; Davis, H., and Lennox, W. G.: The Electroencephalogram in Epilepsy and in Conditions of Impaired Consciousness, Arch. Neurol. & Psychiat. **34**:1133-1148 (Dec.) 1935. Gibbs, F. A.; Lennox, W. G., and Gibbs, E. L.: The Electroencephalogram in Diagnosis and in Localization of Epileptic Seizures, ibid. **36**:1225-1235 (Dec.) 1936. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Cerebral Dysrhythmias of Epilepsy: Measures for Their Control, ibid. **39**:298-314 (Feb.) 1938. Lennox, W. G.; Gibbs, F. A., and Gibbs, E. L.: Effect on the Electro-Encephalogram of Drugs and Conditions Which Influence Seizures, ibid. **36**:1236-1245 (Dec.) 1936. Golla, F.; Graham, S., and Walter, W. G.: The Electroencephalogram in Epilepsy, J. Ment. Sc. **83**:137-155, 1937.

contributions to the possibility of localization of tumors by electroencephalography [5] have been made. However, in only a few instances (notably, those of Foerster and Altenburger,[8] in Germany, and Walter, in England) have direct records from the cortex been demonstrated. We believed that studies on the exposed human brain might give a more accurate idea of the nature of abnormal potentials. The advantages of recording directly from the brain are manifest; the potentials are larger, and the site of activity is available for gross or microscopic study.

At present we have satisfactory records on 22 patients. Numerous records, made at the beginning of this investigation eighteen months ago, have been discarded because of technical defects. In adapting an entirely new and exquisitely sensitive technic to daily use in the operating room many difficulties were bound to occur. Most of these have been overcome through trial and error and we believe that the method which we are now using may be effectively adapted and improved to permit of its more general use in neurosurgical clinics.

TECHNIC

The apparatus which is used in the operating room consists essentially of a three stage, push-pull amplifier, from which amplified potentials may be transmitted to an ink writer or a cathode ray oscillograph. We have used the latter because of its greater sensitivity. The cathode ray unit is freely movable, which permits of greater freedom in the operating room. Deflections on the cathode tube screen can be observed by the surgeon and permanently recorded by a motor-driven camera.

The electrodes consist of 21 gage (0.028 inch [0.71 mm.]) copper wire, coated with amyl acetate–base varnish, except for 1 mm. at the tip, which has been filed to a point. The wire needle is joined to a strand of 36 gage (0.005 inch [0.13 mm.]) insulated copper wire, which runs to a plug inserted in a selector box. This type of electrode prevents change in position of the needles by any unexpected movement of the patient. As many as six pairs of electrodes may be placed in position, and changes in potential between any two leads can be obtained by throwing a selector switch. All connections back to the amplifier are sterilizable.

As yet we have not found it necessary to screen the patient or the operating room. Gross sources of induced 60 cycle alternating current, such as the Bovie diathermy unit and electric heaters, are disconnected from the mains just before oscillographic records are made.

As soon as the operative field is exposed, one of the surgical assistants assembles the sterilized portion of the apparatus. The amplifier and oscillograph have already been connected and "warmed up" for a few minutes. The electrodes are placed on or in the desired area. Usually the grid is on the surface and the ground just

5. (*a*) Walter, W. G.: The Location of Cerebral Tumors by Electro-Encephalography, Lancet **2**:305-308, 1936; (*b*) The Electro-Encephalogram in Cases of Cerebral Tumour, Proc. Roy. Soc. Med. **30**:579-598, 1937. (*c*) Lemere, F.: Berger's Alpha Rhythm in Organic Lesions of the Brain, Brain **60**:118-125, 1937. (*d*) Case, T. J., and Bucy, P. C.: Localization of Cerebral Lesions by Electro-Encephalography, J. Neurophysiol. **1**:245-261, 1938. (*e*) Williams, D. J., and Gibbs, F. A.: Localization of Intracranial Lesions by Electroencephalography, New England J. Med. **218**:998-1002, 1938.

below the cortex, so that in effect electrical activity of all layers of the cortex is recorded. A few seconds are allowed to elapse for stabilization before permanent records are made. In the usual case a series of three or four readings can be taken within a total period of four to five minutes.

The diagnosis in all patients from whom records have been obtained was made on the basis of clinical and roentgenologic findings (including ventriculographic and pneumoencephalographic evidence). Except in 1 case, in which local anesthesia alone was used, all patients were anesthetized with avertin in amylene hydrate supplemented by local infiltration of procaine hydrochloride.

OBSERVATIONS AND COMMENT

Activity of "Normal" Cortex.—In 4 cases frontal craniotomy was performed, in 3 for localized inflammatory lesions of the cisterna chiasmatis and in 1 for cerebrospinal rhinorrhea. In none of the patients was any other lesion demonstrable. Accordingly, records of electrical activity may be considered as coming from "normal" cortex.

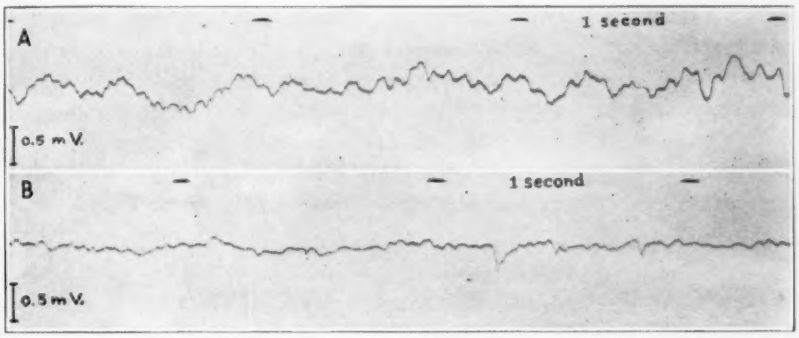

Fig. 1.—Records from the left second frontal convolution of a patient with arachnoiditis of the cisterna chiasmatica. *A*, grid lead on the surface and ground lead below the cortex. There are predominantly waves of beta type (16 to 20 per second; 0.08 to 0.25 millivolt). On these are superimposed swings in potential (6 per second, 0.5 millivolt) which resemble alpha waves, but are slower than the classic alpha rhythm. *B*, electrodes in the deeper cortical layers. The amplitude of beta potentials has been reduced.

In figure 1 *A* are shown the changes in potential typical of those observed in these persons. The record was taken with the grid lead on the surface of the left second frontal convolution and the ground lead below the cortex. Activity of the beta type (16 to 20 per second frequency; 0.08 to 0.25 millivolt amplitude) is present. On this are superimposed larger, slower potentials (6 per second frequency; 0.5 millivolt amplitude) which resemble alpha waves but are of slightly lower frequency than the classic alpha rhythm, which has been described as occurring at a rate of about 8 to 10 per second.

In the same case in which the preceding record was obtained electrical activity from the deeper layers of the cortex was measured. Electrodes were inserted diagonally, so that the uninsulated points lay about 1.5 and 2 mm., respectively, below the surface of the cortex. The record (fig. 1 *B*) shows a much quieter state and a beta rhythm of smaller amplitude (0.05 to 0.15 millivolt) than the preceding record.

The aforementioned records were obtained from the most "normal" patients of our series. The presence of beta potentials agrees with the observations of other workers. The superimposed alpha-like potentials in these cases bring up the question of the origin of alpha activity. Berger [2] maintained that alpha rhythm may be obtained from various parts of the head. Adrian and his co-workers [6] have denied this. Walter [5b] and Lemere [5c] agreed with the latter investigators that alpha rhythm is elaborated by the occipital lobes. More recently, Jasper and Andrews [7] claimed to have found alpha components in the precentral region which seem to originate there and are distinct from the occipital alpha rhythm. We agree with their statement that the precentral region is characterized by a greater proportion of beta potentials than is the occipital region.

The reduction of potential (fig. 1 *B*) when electrodes were inserted in the deeper layers of the cortex is significant. This corroborates the observation of Dusser de Barenne and McCulloch [8] on monkeys and of Bartley, O'Leary and Bishop [9] on rabbits, and illustrates a functional interrelationship of the cortical layers. Since there was no indication to perform a cortical excision in these cases, we could not determine exactly the deeper layers from which diminished electrical activity was recorded. It is our intention to follow this feature of the problem in cases of subpial resection of the cortex for epilepsy.

Increased Intracranial Pressure.—This group consisted of 6 cases of increased intracranial pressure, without primary cerebral tumor. There were 3 cases of suprasellar cyst, 1 of pituitary adenoma, 1 of hydrocephalus and 1 in which the origin was unknown (ventriculographic findings normal). In all cases the presence of increased pressure was verified by clinical, roentgenologic and manometric evidence, and the dura was observed to be very tense at operation.

Comparable records were obtained from the exposed brains of these patients. Figure 2 illustrates electrical activity from the upper part of area 6 in 1 of the

6. Adrian, E. D., and Matthews, B. H. C.: The Berger Rhythm: Potential Changes from the Occipital Lobes in Man, Brain **57**:355-384, 1934. Adrian, E. D., and Yamagiwa, K.: The Origin of Berger Rhythm, ibid. **58**:323-351, 1935.

7. Jasper, H. H., and Andrews, H. L.: Electro-Encephalography: Normal Differentiation of Occipital and Precentral Regions in Man, Arch. Neurol. & Psychiat. **39**:96-115 (Jan.) 1938.

8. Dusser de Barenne, J. G., and McCulloch, W. S.: Some Effects of Laminar Thermocoagulation upon the Local Action Potentials of the Cerebral Cortex of the Monkey, Am. J. Physiol. **114**:692-694, 1936.

9. Bartley, S. H.; O'Leary, J., and Bishop, G. H.: Differentiation by Strychnine of the Visual from the Integrating Mechanisms of Optic Cortex in the Rabbit, Am. J. Physiol. **120**:604-618, 1937. Bishop, G. H., and O'Leary, J.: Components of the Electrical Response of the Optic Cortex of the Rabbit, ibid. **117**:292-308, 1936. O'Leary, J. L., and Bishop, G. H.: The Optically Excitable Cortex of the Rabbit, J. Comp. Neurol. **68**:423-478, 1938.

cases of suprasellar cyst. The potentials have a frequency of 16 to 25 per second and an amplitude of 0.05 to 0.2 millivolt. This corresponds to what has been described as the beta rhythm, and is practically free from other wave forms. Figure 3 *A* is a record taken from the right second frontal convolution in another case of suprasellar cyst. Except for a single large sweep at the beginning of the record, changes in potential are primarily of the beta type. With the electrodes in situ, ventricular puncture was made to reduce the intracranial pressure. A subsequent record (fig. 3 *B*) shows beta rhythm of definitely greater amplitude.

To demonstrate further the effect of pressure, a record from a patient with hydrocephalus is presented (fig. 4). In this case, prior to incision of the cortex for choroid plexectomy, electrodes were inserted through the intact dura to lead

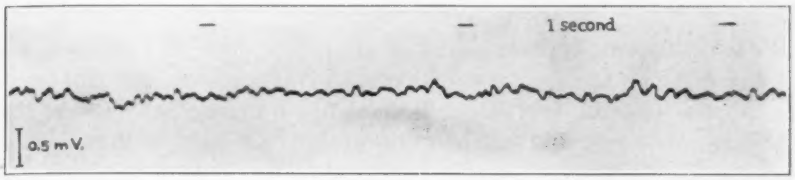

Fig. 2.—Record from the upper part of area 6 of a patient with a suprasellar cyst and increased intracranial pressure. The potentials have a frequency of 16 to 25 per second and an amplitude of 0.05 to 0.2 millivolt; these correspond to the so-called beta rhythm.

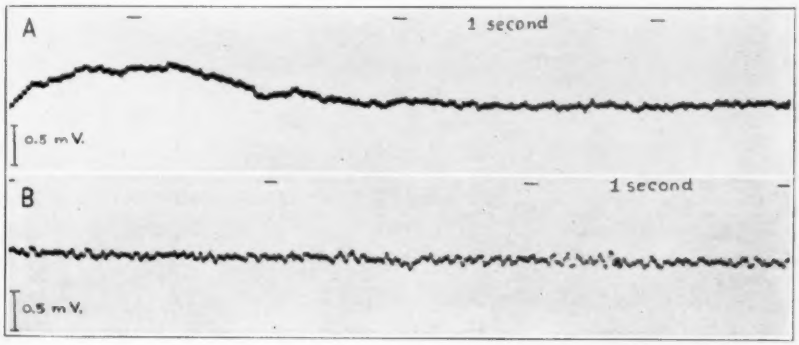

Fig. 3.—Records from the right second frontal convolution of a patient with a suprasellar cyst and increased intracranial pressure. *A*, before ventricular puncture. Except for one large sweep, the potentials are small and primarily of beta type. *B*, after ventricular puncture. There is only beta rhythm, with more distinct changes in potential than before.

from the cortex of the second parietal convolution. There was practically no electrical activity (fig. 4 *A*). Without disturbing the electrodes, a ventricle needle was inserted through the dura at the extreme limit of the field, and 40 cc. of fluid was released. There was almost no change in electrical activity (fig. 4 *B*). After removal of a second 40 cc. of ventricular fluid a dramatic change occurred in the electrical pattern, consisting of marked, irregular activity, with many large

components (fig. 4 *C*). It should be pointed out that the brain in this case was not extremely thin, as is frequent in hydrocephalus; after readings were taken it was necessary to make an incision of about 2.5 to 3 cm. to reach the ventricle.

Characteristic large potentials have not been observed in our cases of increased intracranial pressure caused by lesions other than primary cerebral tumors. This does not agree with the experience of Walter,[5a] who described large waves, differing from alpha waves and having a frequency of 3 to 4 per second and an amplitude up to 100 microvolts (when led from the scalp), occurring in patients with increased pressure or in patients under general anesthesia. It is possible that the discrepancy between his observations and ours may be due to difference in anesthesia.

If the absence of activity before release of pressure in the case of hydrocephalus was due to general depression of function, it is significant that removal of the first 40 cc. of fluid had little or no effect and that the removal of a further amount of fluid produced such a dramatic change in potential. It appears almost as if there is a threshold at which depres-

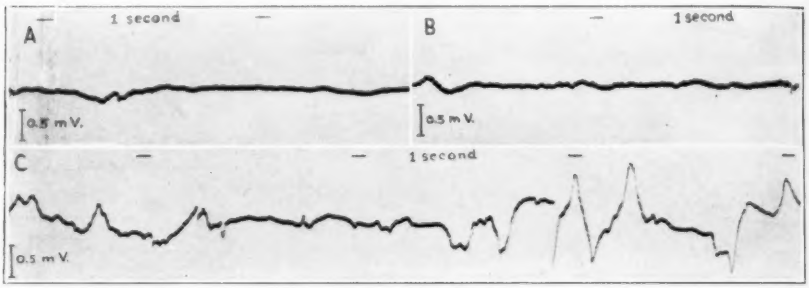

Fig. 4.—Record from the second parietal convolution of a patient with hydrocephalus. *A*, before ventricular puncture. There is almost no demonstrable electrical activity. *B*, after removal of 40 cc. of ventricular fluid. There is little electrical activity. *C*, after removal of 80 cc. of ventricular fluid. The record shows marked, irregular activity, with many large components.

sion is suddenly overcome. If this is true, it is possible that had records been taken continuously we might have observed a progressive building up of potential with the continued removal of small amounts of fluid beyond the initial 40 cc.

So far as the type of potentials is concerned, the records from the frontal cortex in our cases of increased pressure (figs. 2 and 3) show only beta rhythm. This is in contradistinction to the observations of Foerster and Altenburger,[3] who found alpha activity in this area. It is possible that with increased pressure these larger, slower potentials have been abolished. As a matter of fact, the slow, alpha-like potentials which we found in "normal" brains (fig. 1 *A*) are not present in cases of increased pressure.

Activity in Cases of Cerebral Tumor.—The 10 cases of cerebral tumor in this series were divided as follows: Five were of tumors of the frontal region, 1 of the parietal, 1 of the occipital and 2 of the temporal region, and 1 was of the septum pellucidum. Striking patterns of activity were found in these cases. They consisted of potentials which in frequency were similar to the characteristic "tumor" or "delta" waves obtained from the scalp by other investigators.[10]

Figure 5 is a record from the left precentral gyrus, adjacent to a tumor of the frontal lobe. The speed of the camera in this instance was slower than in any of our other cases. The record shows large, slow, diphasic potentials, with a frequency of 2 per second and an amplitude of 1.5 to 2 millivolts for both phases.

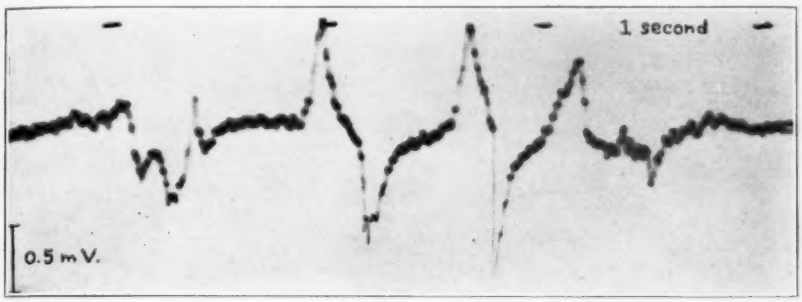

Fig. 5.—Large, slow, diphasic potentials (2 per second) in a patient with a tumor of the left frontal lobe, taken from the precentral arm area, adjacent to the tumor. The speed of the camera in this instance was slower than that in the other records.

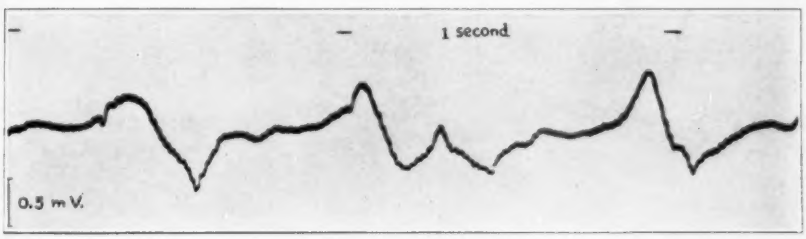

Fig. 6.—Record from the right postcentral arm area, showing characteristic large, slow waves from tissue overlying a deep parietal tumor. There was no demonstrable response to painful stimulation of the contralateral arm.

Records taken with both leads in the body of the tumor showed no electrical activity whatever.

Similar large, slow, diphasic waves were obtained from tissue overlying a deep tumor of the parietal lobe (fig. 6). The electrodes were placed to lead from the sensory arm area. Painful stimulation of the contralateral arm had no effect on the electrical pattern. The operation in this case was performed with the use of local anesthesia alone.

All "tumor waves" are not diphasic. Figure 7 illustrates slow, monophasic potentials from the right occipital pole, overlying an astrocytoma. The same type

10. Walter.[5a, b] Case and Bucy.[5d] Williams and Gibbs.[5e]

of activity was elaborated by tissue overlying a tumor of the temporal lobe (fig. 8*A*). A record taken from tissue 3 cm. distant from the posterior edge of the tumor shows (fig. 8*B*) a series of small, rapid waves, which in frequency and amplitude resemble the classic alpha rhythm.

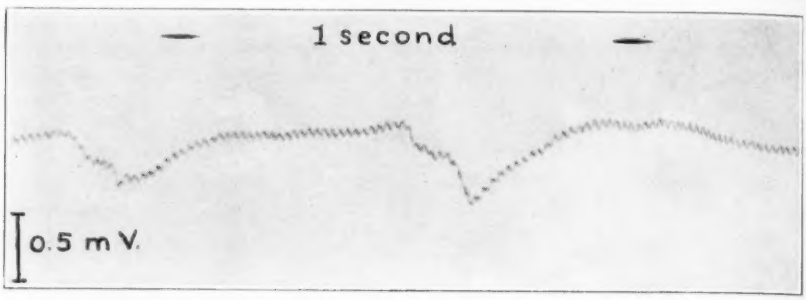

Fig. 7.—Large, slow, monophasic potentials (1 to 2 per second, 0.6 millivolt) recorded from the cortex of the right occipital pole, overlying an extensive astrocytoma.

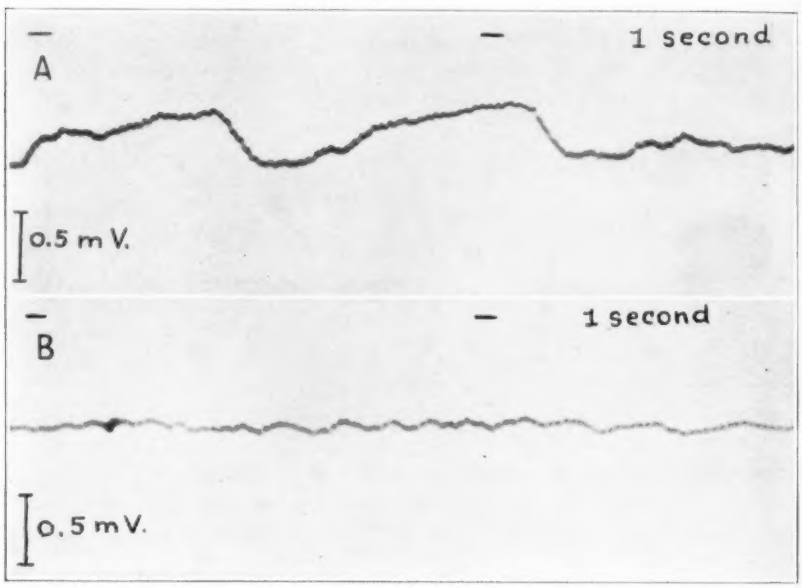

Fig. 8.—Records from the left temporal lobe of a patient with a subcortical spongioblastoma multiforme of the anterior part of the second temporal convolution. *A*, portion of a record from tissue overlying the tumor. A series of large, slow, monophasic waves (1 to 2 per second, 0.3 to 0.5 millivolt) is shown. *B*, record from the posterior end of the second temporal convolution, demonstrating potentials (10 per second, 0.05 to 0.15 millivolt) of entirely different type from those found in the area overlying the tumor.

In figure 9 are shown records from a case of tumor of the septum pellucidum. No tumor had been observed when a right craniotomy was performed elsewhere in 1931, and a course of roentgen therapy was given. At the second operation the posterior portion of area 6 was found to contain scar tissue. With leads in the scarred area irregular potentials were observed, with some waves corresponding in frequency and amplitude to alpha potentials (fig. 9 *A*). With one lead in the scar and the other on the surface of apparently uninvolved tissue anterior to it, very large, slow swings were recorded (fig. 9 *B*).

The origin of the waves in cases of tumor of the brain has not been determined. We, like Foerster and Altenburger [3] and Walter,[5b] have found that tumor tissue itself is electrically inactive. On the basis of our cases we agree with Walter that delta potentials originate not in tumor tissue but in poorly functioning cortex adjacent to tumor and that they "seem to be in the nature of 'inaction' potentials rather than action

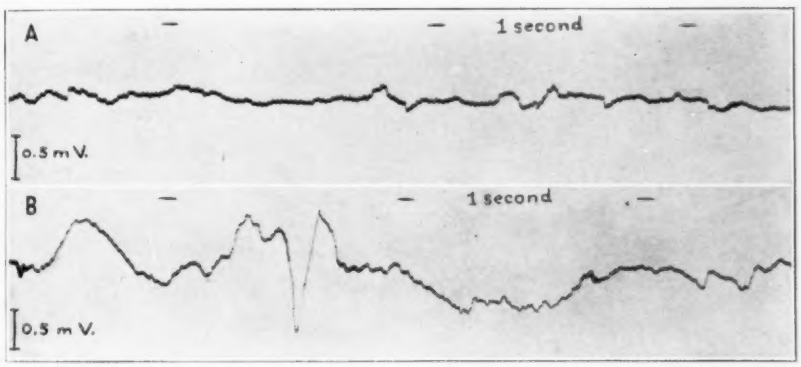

Fig. 9.—Records from a patient with tumor of the septum pellucidum. Area 6 contained some scar tissue, probably caused by craniotomy and roentgen therapy seven years before. *A*, irregular potentials obtained from scarred area, with some waves corresponding in frequency and amplitude to alpha potentials. *B*, a record, taken with one lead in the scar and the other on the surface of uninvolved tissue anterior to it, showing some large, slow swings.

potentials." The absence of large potentials in the scarred area (fig. 9 *A*) and the presence of swings of high amplitude and low frequency between the scar and the apparently normal adjacent brain fit in with this hypothesis. On the other hand, the absence of these abnormal components in cases of increased pressure not due to tumor suggests that the phrase "poorly functioning cortex" must be qualified to include varying degrees of malfunction. It may be assumed theoretically that in cases of increased pressure (e. g., hydrocephalus) the entire cortex is equally depressed (or stimulated), with the result that any change in potential in one area occurs in equal degree elsewhere, so that differences in potential between any of several areas remain unchanged. In cases of tumor or

scar, however, the depressive (or irritative) effect of the lesion is primarily directed locally, so that, without similar effect elsewhere in the brain, the difference in potential between tissue adjacent to the lesion and the remainder of the brain is increased.

In the record from the postcentral gyrus (fig. 6) the absence of a demonstrable response to painful stimulation of the contralateral arm is disappointing. Sensory action potentials have been obtained in animals by Marshall, Woolsey and Bard [11] and by Bartley and Heinbecker.[12] It is possible that the high tumor potentials may have masked any such response, or that the tumor itself may have blocked the impulse.

The absence of alpha rhythm in tissue overlying a tumor of the occipital lobe (fig. 7) is significant. Lemere,[5c] who agreed with Adrian

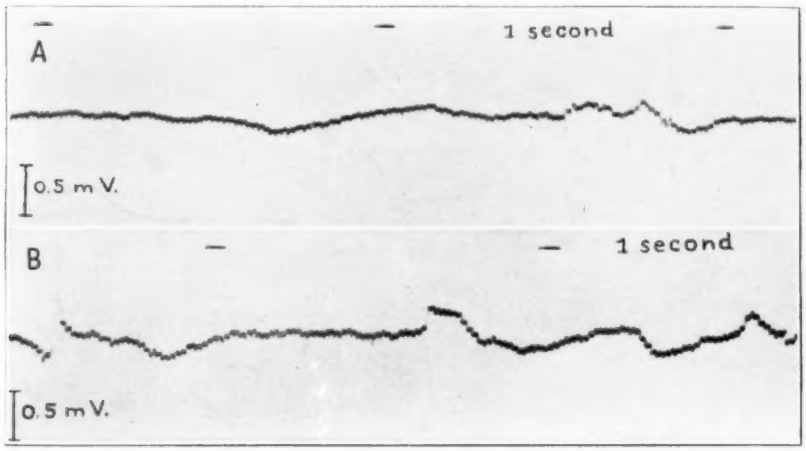

Fig. 10.—Records from the left cerebellar hemisphere in a case of Ménière's disease. *A*, from the superior semilunar lobule. Only brief changes in potential of no characteristic type are demonstrated (compare with figure 11 *B*). *B*, from the same lobule but with leads situated more medially, almost at the vermis. There is more activity, but no constant wave form.

and his co-workers [6] that alpha potentials are produced in the occipital lobe, has found increased alpha rhythm on the side of a lesion in records obtained from the scalp. The record in this case, like that in case 2 reported by Case and Bucy, does not coincide with Lemere's observations.

Cerebellar Activity.—We have two records from the cerebellum. They are of interest because of the relatively small number of similar records published [13] and because they themselves offer an interesting comparison.

11. Marshall, W. H.; Woolsey, C. N., and Bard, P.: Cortical Representation of Tactile Sensibility as Indicated by Cortical Potentials, Science **85**:388-390, 1937.

12. Bartley, S. H., and Heinbecker, P.: The Response of the Sensorimotor Cortex to Stimulation of a Peripheral Nerve, Am. J. Physiol. **121**:21-31, 1938.

13. Foerster and Altenburger.[3] Walter.[5]

Figure 10 *A* shows the record from the left superior semilunar lobule in a patient operated on for Ménière's disease. There is relative inactivity, with only brief changes in potential of no characteristic type. With electrodes situated more medially, almost at the vermis, more activity is present, but again there is no constant wave form (fig. 10 *B*).

Records have been obtained from the superior semilunar lobule overlying a deep-seated tumor of the left cerebellar hemisphere. Figure 11 *A* shows large, irregular changes in potential. With leads in the adjacent lamella, corresponding in position with the leads in the preceding case (fig. 10 *A*), a curious discharge of paired waves, not synchronous with the pulse, was observed (fig. 11 *B*).

With only 1 case of cerebellar tumor it is not possible to evaluate the localizing significance of the high potentials recorded in figure 11 *A*. Any possible generalizations are limited to a comparison of figures 10 *A* and 11 *B*. The electrodes were situated in the same position in each instance. The relative inactivity in the first record is in sharp con-

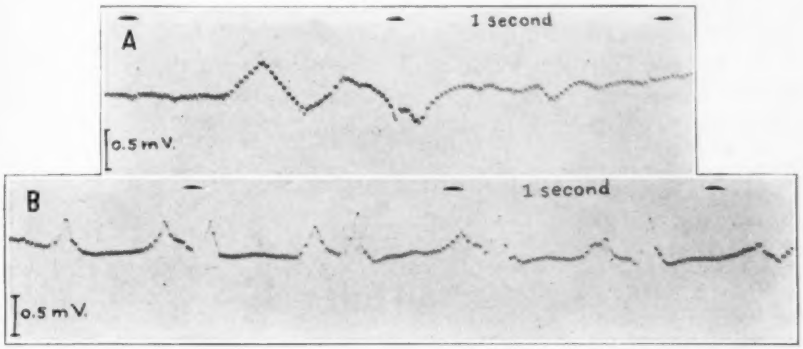

Fig. 11.—Records from the cortex overlying a tumor of the left cerebellar hemisphere. *A*, from the superior semilunar lobule, showing large, irregular wave form. *B*, from the same lobule, but leading from a point corresponding to the site from which the record in figure 10 *A* was obtained. This record is made up of an unusual series of regular, paired waves.

trast to the changes in the record obtained in the case of tumor. In the latter the discharge of a series of paired waves is a prominent feature. It suggests that there may be two foci discharging almost equal monophasic impulses at a rhythm of approximately 2 per second, either just out of phase with each other or with the first of the pair acting to "fire off" the second.

SUMMARY

A method is described whereby action potentials may be recorded from the exposed human brain under the aseptic conditions of the operating room.

The records obtained in a mixed series of 22 cases are briefly discussed.

Records from the frontal cortex of 4 patients with "normal" brains in which no space-occupying lesion was present are characterized by activity of the beta type. Reduction of potential was observed when electrodes were inserted in the deeper layers of the cortex.

Large potentials were not observed in 6 cases of increased intracranial pressure without primary cerebral tumor. In 1 case of hydrocephalus high potentials were noted only after release of ventricular fluid.

In 10 cases of cerebral tumor characteristic waves of high amplitude and slow frequency were observed in tissue overlying or adjacent to the tumor. Tumor tissue itself is not electrically active but apparently exerts an effect only through functional change in the surrounding brain.

A comparison is made of activity from tissue overlying a cerebellar tumor and that from a similar area in a case of Ménière's disease.

The aforementioned observations suggest as possibilities for further investigation: (1) more precise localization of potentials in the layers of the cortex; (2) the association of large potentials with normal activity observed elsewhere in the brain, and (3) the relation of the abnormal waves to the response to sensory stimulation.

Dr. George H. Bishop gave valuable aid in this investigation.

DISCUSSION

Dr. F. A. Gibbs, Boston: The authors are to be congratulated on having continued a type of study that appears to have been abandoned after Foerster and Altenburger reported on the subject. Berger was the first to record directly from the human brain. He reported that there is no electrical activity of the alpha type in cases of tumor of the brain. This was then and is now an exceedingly important observation.

The present authors concern themselves with localizing tumors at operation. Although this is desirable, one should remember that it is more important to find where the tumor is before operation. The question of exactly what type of activity comes from the area over a tumor and from the boundaries of a tumor is exceedingly interesting. It is true, however, that both normal and abnormal activity comes through the intact skull. One should make sure, therefore, that one is not recording from the exposed brain what can be more easily and perhaps more accurately recorded from the unexposed brain.

What can be done with this technic and what cannot be done on the unexposed brain is to sharply delimit the boundaries of a tumor. Perhaps Dr. Schwartz has tried to do this. With this technic it is also possible to lead off from the depths of the brain, from the thalamus, for example, and from the lower centers. This is an important study which it is hoped these authors will undertake.

By working directly on the brain it is possible to study the functional organization of the cortex at the microscopic level, as Forbes and his co-workers are doing, and at the more nearly macroscopic level, as is illustrated by the work of Dusser de Barenne and McCulloch and by that of Bard and Marshal.

Dr. Paul C. Bucy, Chicago: I have real hopes that this new technic which Dr. Schwartz and his colleagues have reintroduced, along with such experimental

technics as those of O'Leary and Bishop, will help to extend knowledge and to elucidate more fully the field of electroencephalography. I think it is important to realize that at present one is dealing with electroencephalography in an empiric manner, with relatively little knowledge or information. Tracings of electric potentials are being made from the intact skull in the majority of cases, and attempts are being made to correlate them with certain clinical conditions or pharmacologic situations, with little understanding of what is actually being measured or recorded.

It is of interest, of course, that it has been possible to correlate the findings with certain clinical observations and that continued observations have adequately supported the original observations of Walters and of my colleagues and myself that tumors can usually be localized by this technic; but that is aside from the point. One should bear in mind that in the ordinary electroencephalogram two electrodes are applied at a considerable distance from one another on the skull and that what is measured is not one single change in potential but a summation of the millions of alterations in potential which occur between the two electrodes. And until one knows what those changes in potential are, what they represent and where they originate, one knows nothing about electroencephalography. It is my hope that the type of technic presented today will advance knowledge in that field and direction.

Dr. Henry G. Schwartz, St. Louis: Dr. Gibbs's point about Berger's original investigations on the explored brain is well taken. As he said, Berger found no electrical activity in a tumor of the brain. That has also been our experience. My especial emphasis on the paper of Foerster and Altenburger was due to the fact that they were really the first to present a sufficiently large series that could be studied.

I had hoped that I might not give the erroneous interpretation or impression that our interest was primarily to delimit tumors. We have taken the cases as they have come. It is impossible, of course, when dealing with human beings to choose and pick as one can in the experimental laboratory. In the course of our observations we have only incidentally delimited tumors. We have also in one case in which a tumor was suspected proved electroencephalographically that no tumor waves were obtained in the exposed area; at a subsequent operation, when correct exposure was made, a tumor was found.

In regard to Dr. Gibbs's point about activity from the depths of the brain, I have purposely not touched on that subject. At present we have only two records, one from the thalamus and one from the caudate nucleus, from which we can make no generalizations, but that is in our program.

With regard to Dr. Bucy's statements and the hope that we might find the source and mechanism of potentials, we have had only a little opportunity to study this. I reported 1 case in which the electrodes were placed within the deeper layers of the cortex, probably between the third and the fifth layer. The potentials from this region were small, and it is apparent that they constitute only one component of the potentials obtained when one leads from the entire thickness of the cortex. This observation fits in with those of Bishop and his co-workers. Unfortunately, in that case there was no indication for excising the tissue for microscopic study, since the patient had a lesion around the chiasm; but in those cases in which cortical excisions for epilepsy are made, for example, we are looking forward to obtaining specimens of tissue and finding out just where our electrodes have been placed in the layers of the cortex.

Case Reports

METRAZOL TREATMENT OF THE PSYCHOSES

Report of Two Deaths

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We shall not discuss the advantages or disadvantages of the metrazol treatment in this paper, but report 2 cases of deaths which in our opinion were unusual and unexpected.

The method of administration is well known and will not be discussed here. Briefly, we used the standard 10 per cent solution of metrazol intravenously on alternate days, three times a week. Breakfast was omitted on treatment mornings, and in its place we gave 300 cc. of a 40 per cent solution of sucrose. The initial dose of metrazol was usually between 2 and 4 cc., depending on the body weight, and this was gradually increased by about 0.3 to 0.5 cc., in order to obtain a grand mal seizure with each injection.

REPORT OF CASES

CASE 1.—P. H., a white man aged 56, married, was admitted to the Columbus State Hospital on Aug. 12, 1938, in a rather poorly nourished condition. His father had died of purpura haemorrhagica at the age of 42. His mother had manifested hysterical reactions during her life and had died at the age of 67, of "kidney trouble."

There was nothing of importance in the history of the patient's childhood. His wife described him as a good husband, a good provider and a likable, jovial person who took part in community affairs. He seemed outwardly happy, but had a tendency to worry about trifles and nonessentials. He was a salesman and the father of 3 children. Ten years before admission he bruised his right foot, with resultant osteomyelitis of the metatarsal bones. This was successfully treated surgically. He was said to have had hypertension for several years and to have smoked excessively most of his life.

In May 1938 a new firm took over his employer's company, and this caused him to fear loss of his job. He made an effort to create a good impression, but resigned on May 26 because he could not think clearly. Soon after, he was unable to sleep. Persecutory ideas developed. He told his wife "they" were going to accuse him of misappropriating funds, "frame" him and send the police after him. A stay in a private sanatorium for two weeks did not improve his condition. He became so restless that he was admitted to the state hospital.

Physical Examination.—The heart was essentially normal. The blood pressure was 175 to 185 systolic and 105 diastolic. The radial arteries were thickened, but easily compressible. The dorsal part of the right foot showed an old healed operative scar. Neurologic examination gave normal results. The patient did not cooperate in examination of the eyegrounds. Laboratory determinations showed nothing abnormal.

Mental Examination.—The patient was extremely agitated and depressed. He moaned and groaned frequently. He answered questions in as few words as possible. He expressed the delusions already mentioned. There was evidence of defects of memory and orientation, but little, if any, deterioration.

Diagnosis.—The diagnosis was involutional psychosis, melancholia.

Course.—The agitated depression continued. The patient was often seen in his room with his hands over the trachea, squeezing hard enough to mark the neck. No improvement was noticeable with the usual forms of therapy.

Therapy.—Metrazol treatment was started on September 20. The patient had three grand mal seizures, without ill effect. The fourth injection was given on September 28, and this also resulted in a typical convulsion, lasting fifty seconds. On regaining consciousness he complained of severe pain in the left leg and would not permit any one to touch it. Examination revealed the left lower extremity below the knee to be cold, blanched and tender on touch or movement. The muscles of the calf were flabby and seemed to be drawn up in a bundle. The dorsalis pedis pulse was absent.

A consulting surgeon suggested the possibility of thrombosis of the femoral artery and advised amputation. On September 29 the left lower extremity was amputated at the junction of the middle and the upper third of the thigh. The femoral artery did not bleed at the site of operation and was filled with a blood clot.

On the next day the patient seemed much better mentally, but on October 1 the temperature became elevated, and gradually rose to 103.8 F. At the insistence of his wife, he was transferred to a general hospital, where he died on October 4. Autopsy was not permitted. The attending physician at the hospital stated that he died of pulmonary embolism.

Comment.—The clinical diagnosis was endarteritis obliterans, or Buerger's disease. The femoral artery was partially occluded by a white, canalized thrombus. Microscopic sections showed a slight degree of internal sclerosis.

No history of Buerger's disease was given at the time of admission. The wife later admitted that the patient sometimes complained of pain in the calf of the left leg which was severe and cramplike. This led us to believe that the disease existed before the treatment.

Beckman[1] described Buerger's disease as "an inflammatory infection of the deep-seated arteries and veins and the superficial veins of the lower extremities, occasionally of the upper extremities." The cause is unknown, but allergic sensitiveness to tobacco is often mentioned. Toxic or bacterial exciting factors have been suggested. The disease occurs principally in middle-aged male Jews.

This patient was an excessive smoker, but a Gentile. The thrombosis of the left femoral artery apparently occurred during or immediately after the convulsive seizure. Exactly what happened is not clear to us. The production of a temporary spasm of the artery, injuring the vessel wall and thus producing a thrombus, may be considered a partial explanation. It is known that spontaneous thrombosis of a main artery may occur. It may be that the accident was purely coincidental. One of us has observed the same thing in an agitated arteriosclerotic patient who had not been subjected to metrazol therapy.

CASE 2.—M. F., a white woman aged 32, was admitted to the Columbus State Hospital on Oct. 7, 1938. She was the youngest of a family of 4 children. Two

1. Beckman, H.: Treatment in General Practice, ed. 2, Philadelphia, W. B. Saunders Company, 1934, p. 550.

older sisters had always protected and guided her, as she was backward even as a child. It was six weeks before she would speak out loud when she started school. She was never sociable and found it difficult to meet people. As a child she was frail, but otherwise healthy. At college she was an "A" student and a member of three honorary societies. A fellowship for additional study was never used. Thyroidectomy was performed in 1928. Recovery was uneventful, although the informants dated the present illness from that time.

After the operation, the patient began to have peculiar sensations in her body. She had delusions that her muscles were fluid, that her chest was a pool of water, that she did not have a diaphragm and that her nerves were broken in two. At times she believed that her mother and sisters were against her and that her food was poisoned. She was cared for at the home of a sister until her admission to a private sanatorium, six weeks before entrance to this hospital. A letter from her home physician gave the additional information that she was impulsive and subject to temper. During the time she was under his care paranoid ideas were outstanding.

Physical Examination.—On admission the signs were not remarkable. The blood pressure was 114 systolic and 80 diastolic. She had mild anemia (with a red cell count of 3,950,000), which was improved by administration of reduced iron (red cells, 4,150,000).

Mental Examination.—The patient was listless and disinterested, although fairly agreeable and cooperative. She complained of easy fatigue and the various somatic ailments mentioned previously. Memory, orientation and general knowledge were normal. She was reluctant to admit actual delusions about her family, saying only that they did not understand her. There was the belief that radio programs "were arranged for her benefit." She was evasive about hallucinations, but did say that she could sense ideas and heard peculiar noises when she was very sick.

Diagnosis.—The diagnosis was dementia praecox, hebephrenic type.

Therapy and Course.—Insulin treatment was instituted on Nov. 5, 1938, and terminated on Jan. 17, 1939. A total of forty-two treatments were given, with thirty-five shock or coma doses. The highest dose producing coma was 155 units and the lowest 130. Paranoid ideas rapidly decreased, and the patient became more cooperative. In the occupational therapy department it was noted that she became progressively more able to carry on activity, but lacked initiative. During psychotherapeutic sessions it was found that this was due to her feeling of inadequacy. She felt she lacked the physical energy to carry any given task to its completion.

Metrazol convulsions were induced on January 23 and 25. She was admitted to the hospital ward after the second treatment, as she felt faint and complained of a vaguely localized pain in the upper portion of her back. Two days later the pain shifted to the upper lumbar region and was still poorly localized, although there was a suggestion of muscle spasm at the right of the vertebral column. From January 27 to February 2 there was a daily variation in temperature of from 101 to 104 F. From February 2 to 6 the temperature continued between 103 and 105 F., finally rising to 106 F. on the day of her death. The urine, examined repeatedly, was normal at first. On February 1, 3 and 7 there was only 40 mg. of albumin with from 30 to 40 leukocytes per high power field. The white blood cells on January 28 numbered 6,950, with 61 per cent polymorphonuclears; on February 1 the count was 10,850, with 79 per cent polymorphonuclears, and on February 6, 19,850, with 85 per cent polymorphonuclears. A loud systolic murmur was first noted on February 4. A diagnosis of acute

bacterial endocarditis was established on the following day by the appearance of capillary thrombi in the fingers and conjunctiva, in addition to a tender, swollen spleen. At the same time a culture of the blood taken seventy-two hours before was reported to yield staphylococci. On February 7, the day of her death, the pulse rate, which had varied between 100 and 140, rose to 150, and then became imperceptible. Treatment consisted of two transfusions of 250 cc. of citrated blood on February 2 and 4, with administration of large doses of sulfanilamide until the blood culture was reported to yield staphylococci. Additional supportive treatment was given in the form of parenteral fluids.

Pathologic Observations.—The heart weighed 275 Gm. and presented a smooth, glistening surface. The myocardium was fairly firm and pink, with occasional tiny grayish scars. The mitral valve showed considerable beading along its margin of closure, and at one point a large vegetation was embedded in a strand of clot. The aortic valve showed only a few atheromatous plaques. Other valves were normal. The coronary arteries were normal. The lungs weighed 400 Gm. and were normal. The spleen weighed 350 Gm. and was covered with fibrin; the surface was mottled and varied from bright red to purple; normal architectural markings were lost, owing to multiple infarctions. The liver weighed 1,400 Gm. and showed an area in the right lobe which resembled an infarct. The gallbladder, adrenal glands and pancreas were normal. The ileum showed an area of purplish discoloration, about 2 cm. in diameter. The kidneys weighed about 125 Gm. each and presented many tiny patches which were found to be abscesses. There was a triangular infarct in the cortex of the right kidney, about 1 cm. in diameter. The bladder and reproductive organs were grossly normal. Permission for examination of the head was not obtained.

Microscopically, the heart showed multiple pyogenic abscesses, with healed and active Aschoff bodies. The spleen, liver and intestine showed abscesses in the areas previously mentioned. A Gram stain of the organs revealed bacteria resembling staphylococcic.

Diagnosis.—The diagnosis was: (1) acute bacterial endocarditis; (2) septic emboli, with abscesses in the heart, liver, spleen, kidneys and intestine, and (3) recurrent acute rheumatic fever.

Comment.—As there was no history of cardiac disease, the sisters were questioned further after the diagnosis of acute bacterial endocarditis was made. They referred vaguely to a "cardiac condition" at the time of the thyroidectomy. The clinic where this operation had been performed reported that the patient had returned about a year later with acute endocarditis, of undetermined origin.

It is difficult to understand the part which metrazol may have played in the production of the endocarditis. The sequence of events seems to show too definite a relation to be coincidental. It has been suggested that the convulsions may have caused a vegetation to break loose. The thrombus which produced the infarct in the right kidney may have been the cause of the early pain in the back.

CONCLUSIONS

In our opinion, metrazol apparently played an important part in the 2 deaths.

Metrazol convulsions should never be induced in the presence of cardiovascular disease. Because of the difficulty of obtaining an accurate history in cases of mental disease, an electrocardiogram should be a routine procedure before metrazol treatment.

SPONTANEOUS HEMORRHAGE INTO OCULOMOTOR NERVE WITH RUPTURE OF NERVE AND FATAL SUBARACHNOID HEMORRHAGE

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Isolated unilateral paralysis of the oculomotor nerve may be caused by a variety of pathologic processes. Not infrequently it is due to compression of the nerve by hemorrhage from an aneurysm of the circle of Willis. Hemorrhage within the nerve itself, however, is extremely rare. The following case of disrupting hemorrhage into the third nerve with resulting subarachnoid hematoma, therefore, seems worth reporting.

REPORT OF A CASE

B. H., a white man aged 65, unemployed, was admitted to the neurologic service of the Beth Israel Hospital on Nov. 11, 1933,[1] complaining of headache, vomiting and drooping of the right upper eyelid. It was said that there had been slight drooping before. The past history was not contributory. Except for lobar pneumonia, six years prior to admission, the patient had always enjoyed good health. Four weeks before entering the hospital, while drinking coffee in a restaurant, he suddenly became unconscious and fell to the floor. Unconsciousness lasted for about half an hour and was followed by severe headaches. The headaches were dull and aching in character and occurred at any time. They were most marked over the vertex and the right occipital region. One week later the patient began to have attacks of nausea, and vomited two or three times a day. The vomiting was not projectile, and relieved the headaches. At the same time the patient noticed increasing difficulty in raising the right eyelid, which now drooped constantly. He complained also of occasional buzzing in his ears, of occasional sharp pains in the thighs and of continuous drowsiness.

Examination.—The patient was well nourished and well developed, with slight hypertension (blood pressure 160 systolic and 90 diastolic). The urine gave a 2 plus reaction for albumin, and there were occasional granular casts.

The positive neurologic findings were: (1) slight nuchal rigidity, slight Brudzinski sign and a Lasègue sign bilaterally; (2) paralysis of the right oculomotor nerve; (3) loss of the right triceps reflex, exaggeration of the right knee jerk and loss of the left achilles reflex; (4) drowsiness, euphoria and slight mental confusion.

Ophthalmologic examination of the right eye revealed that the oculomotor nerve was paralyzed and the fundus was not visible; that of the left eye showed choroidal hemorrhages and sclerotic vessels.

The pulse, temperature and respiration were normal throughout the patient's stay in the hospital. The blood count revealed no abnormalities. The blood contained 143 mg. of dextrose and 50 mg. of nonprotein nitrogen per hundred cubic centimeters. The Wassermann reaction of the blood was negative. Roentgen examination of the skull gave normal results except for diminished aeration of

From the Pathological Laboratory, Beth Israel Hospital.

1. Dr. E. D. Friedman permitted use of the clinical data.

the right ethmoid and sphenoid sinuses. Lumbar puncture yielded definitely xanthochromic fluid under a pressure of 500 mm. of water. There was no blood.

Course.—After twelve days the patient was discharged as improved, with a diagnosis of subarachnoid hemorrhage due to leakage from an aneurysm of the right carotid or posterior communicating artery.

Three weeks after discharge the patient was readmitted to the hospital. In the interval he had suffered from attacks of severe headache in the right frontoparietal region. Twenty-four hours before admission he suddenly lost consciousness and fell, cutting his left upper eyelid. He had remained in coma since, with occasional twitchings of the extremities, and could be aroused only with difficulty. He vomited repeatedly; the head, neck and extremities were held rigid. He breathed noisily and was cyanotic most of the time.

When reexamined the patient was stuporous. There was Cheyne-Stokes respiration. Ankle clonus was present bilaterally. The reflexes were active and symmetric. There was marked nuchal rigidity, and the Brudzinski and Kernig signs were positive. The right oculomotor nerve was completely paralyzed. There were conjugate deviation of the eyes to the right and absence of the light reflexes. Questionable weakness of the right side of the face and the right arm and occasional twitchings of the right arm and the left leg were noted.

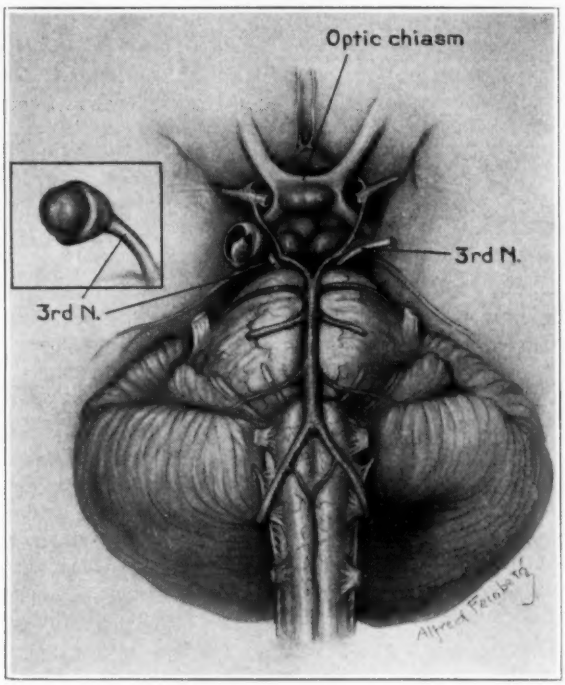
A spinal tap revealed xanthochromic fluid and the presence of fresh blood. The pressure was 320 mm. of water. The blood pressure was 220 systolic and 120 diastolic. The urine gave a 4 plus reaction for albumin and contained numerous hyaline and granular casts. The nonprotein nitrogen content of the blood was 55 mg. per hundred cubic centimeters. The pulse rate varied from 50 to 80 per minute. The temperature ranged from 99 to 100 F. for the first three days; on the fourth day it rapidly rose to 106.2 F., and the patient died without regaining consciousness.

Autopsy.—The anatomic diagnosis was: hemorrhagic destruction of the right oculomotor nerve; subarachnoid hemorrhage; large hemorrhagic focus in the anterior lobe of the hypophysis; chronic internal hydrocephalus; generalized, moderately severe atherosclerosis; hydropericardium; dilatation of the right auricle; moderate hypertrophy of the left ventricle; pleural adhesions; apical scars; cheesy focus in the apex of the left lung; emphysema; parenchymatous change in the liver, kidneys and myocardium; duodenal scar; exostoses of the spinal column; cataract of the right eye.

Gross Appearance of Brain: The brain was removed during the night by an intern; unfortunately, no attention was given to the distal portion of the oculomotor nerve. Examination of the eyes was not feasible. The brain was of normal size, and the soft meninges were considerably congested over the cerebral hemispheres. A subarachnoid hemorrhage occupied the left mesial aspect of the base, the temporal and occipital lobes, the cerebellum and the cisterna ambiens. The circle of Willis was obscured by the hemorrhage. In the region where the aneurysm was suspected an aneurysm-like, bluish mass, the size of a pea, was observed. After careful removal of the clotted material from this region, it could be seen that all the branches of the circle were intact and that none of them was connected with the aneurysm-like mass previously described. In the process of dissection the tip of the mass came off. This tip had a thin grayish wall and inside seemed to be composed entirely of blood clot. It further became evident that the posterior cerebral, the superior cerebellar and the pontile branches were not connected with this formation. While the left oculomotor nerve was normal, the right oculomotor nerve could not be found at all, and the position of the aneurysm-like

mass corresponded exactly to that of the right oculomotor nerve; it was attached to the brain by means of a pedicle which did not look unlike nerve tissue. The basilar and vertebral arteries showed nothing unusual.

After the tip had broken off, the aneurysm-like lesion could be seen more clearly. It became thicker toward the brain and had an outgrowth laterally and posteriorly. The whole formation was about the size of a large pea, the outgrowth about that of a large grain of rice. The length, including the broken-off tip, was about 8 mm. This measurement was taken from a distinct furrow which separated the sac proper from the nervelike pedicle previously mentioned. This pedicle was flat, having a slightly convex contour anteriorly and mesially and a correspondingly



Proximal stump of the severed oculomotor nerve as it appeared after removal of the blood clot. The insert represents reconstruction of the stump before it was broken. The breaking happened during removal of the blood clot.

Note the normal condition of all the branches of the circle of Willis and of the other basilar vessels.

The drawing also indicates the distention of the infundibulum.

concave contour on the opposite side. Its transverse diameter was 3 mm.; the other, about 1.5 mm. The furrow mentioned could be seen distinctly on the convex surface. The concave surface was obscured by the hemorrhage, which could not be removed because there was danger of tearing off the pedicle.

A horizontal cut through the brain revealed much widening of all the ventricles. The widening was symmetric and even. In the left anterior horn adhesions were seen at the lateral upper aspect. The ependyma was deeply injected, and there

were fine brownish masses, probably remnants of hemorrhage, which could be scraped off easily. The infundibulum was wide. Its walls, notably in the lower portion, were very thin. The choroid plexus showed a high degree of cystic change, notably in the posterior horn. The fourth ventricle was wide also. Hemorrhage was abundant in the soft meninges, below the cerebellum and on the neighboring portions of the hemispheres.

Microscopic Observations: A small piece from the pedicle of the aneurysm-like formation, i. e., from the proximal portion of the oculomotor nerve, consisted of nerve tissue with hemorrhage at one end. The nerve tissue was inflamed. The endothelial cells of the blood vessels had swollen nuclei. Medium small, irregularly round cells with dark nuclei formed rather loose heaps around the blood vessels. In longitudinal sections they were seen to accompany the vessels.

A section from the broken-off tip revealed only a thin layer of tissue surrounding the hemorrhage. In the basal portion of the nerve the Bielschowsky stain showed the usual network. A similar network could be demonstrated by the silver stain in the thin layer of tissue surrounding the hemorrhagic portion of the tip. The meshes obviously were elongated, and the nerve tissue was difficult to recognize. Characteristic nuclei were seen. The cystic plexus choroideus contained many corpora amylacea. The ependyma for the most part was normal. There were small protrusions of neuroglial tissue. Directly under the ependyma a number of small, occluded, fibrotic blood vessels were seen, while the neighboring vessels were normal.

Several sections were taken from different portions of the brain. A number of small hemorrhages were observed under the ependyma of the lateral ventricle on one side. In the same region rather large ependymal granulations were seen. There was hyaline thrombosis in a number of capillary vessels deep in the brain substance. At many points the thin layer of blood in the soft meninges contained scattered leukocytes. There was, however, no evidence of a true meningitic process.

In the surroundings of the middle cerebral artery some inflammation was observed. The cells were small, perhaps shrunken; about half of them seemed to be polymorphonuclear leukocytes.

The hypophysis was examined in serial sections. In the upper third of the anterior lobe a large area, occupying about two fifths of the horizontal section, was destroyed by hemorrhage and inflammation. No blood vessel responsible for the hemorrhage could be found. The area was situated in the posterior portion of the anterior lobe. It surrounded the stalk and had partly destroyed the pars tuberalis.

REVIEW OF THE LITERATURE

An extensive search for similar cases was made in the American and the foreign literature. The textbooks do not even mention the possibility of paralysis due to intraneural hemorrhage. Only Oppenheim,[2] in discussing the causes of palsies of the oculomotor nerve, wrote: "Primary hemorrhage within the nerve occurs but rarely." He himself observed a case of transitional paralysis of the fourth cranial nerve in a young man with profuse epistaxis and expressed the opinion that it was due to intraneural hemorrhage.

2. Oppenheim, H.: Lehrbuch der Nervenheilkunde, ed. 7, Berlin, S. Karger, 1923.

Similar views were expressed by Calhoun.[3] One of his patients, a woman aged 44, suffered from periodic headaches, which occasionally were combined with temporary amaurosis. This, according to Calhoun, may have been caused by hemorrhage into the nerve sheath. These observations, however, were clinical and were not confirmed by pathologic examination.

The title of an old dissertation for a doctorate (Stiebel,[4] 1847) evoked the hope that we might finally have found a parallel to our observation. The description, however, suggests abscess of the brain or subdural abscess.

Sänger,[5] in 1880, reported the case of man aged 31 who had died with the signs and symptoms of basal meningitis. At autopsy a gelatinous exudate, with many tubercles, was observed at the base of the brain. The left oculomotor nerve was considerably thicker than the right and showed diffuse, deep red discoloration, which extended from the point at which the nerve left the crus cerebri to the superior orbital fissure. Cross sections revealed that the nerve was not round, but irregularly oval. There were four confluent hemorrhagic areas. The hemorrhage was more marked toward the periphery, thus rendering the nerve club shaped. The nerve fibers were flattened. There was slight infiltration with round cells around some vessels. The perineurium was normal. Veins at the proximal portion of the nerve were thrombosed. The latter change, in the presence of normal arteries, was, according to Sänger, the cause of the circulatory trouble.

The same author described a hemorrhage into the left oculomotor nerve in another case of tuberculous meningitis. A man aged 26 had presented, besides general meningeal symptoms, ptosis and then complete paralysis of the third and fourth cranial nerves on one side. The form of the hemorrhage led Sänger to suspect a hemorrhage into a lymph space. He also observed blood pigment in some places, which he considered a sign of previous extravasation.

Recently, Gurdjian and Bailey[6] reported a case of paralysis of the third cranial nerve due to spontaneous hemorrhage within the nerve in its intracranial course. A woman aged 34, a cornet player, came to the hospital because for one week she had been unable to open the right eye. She also complained of pain in the right temple and right side of the forehead and of vertigo. The symptoms had increased in intensity in the last days. The patient had never been ill before. Three of her sisters had died of hypertension between the ages of 34 and 48 years. Examination revealed complete paralysis of the right oculo-

3. Calhoun, F. P.: Ocular Symptoms of Subarachnoid Hemorrhage, J. A. M. A. **87**:1104 (Oct. 2) 1926.

4. Stiebel, F. J.: Paralyseos haemorrhagicae nervi oculomotorii in infante observatus casus rarissimus, Thesis, Heidelberg, Frankfurt, J. D. Sauerlaender, 1847.

5. Sänger, M.: Oculomotoriuslähmung bei Meningitis tuberculosa adultorum durch periphere und zentrale Blutung, Arch. f. Psychiat. **10**:158, 1880.

6. Gurdjian, E. S., and Bailey, L. J.: Paralysis of Third Cranial Nerve Due to Spontaneous Hemorrhage Within Nerve in Latter's Intracranial Course, J. Nerv. & Ment. Dis. **84**:61, 1936.

motor nerve. Otherwise the findings were not abnormal. Laboratory examination of the blood, urine and spinal fluid gave normal results. The patient was discharged after one week in the hospital, only to be readmitted at the end of one month. During this interval she had been relatively well. Then, suddenly, she experienced a severe headache and an hour later became disoriented. On the next day she presented mild opisthotonos, complete paralysis of the third nerve and a questionable Babinski sign bilaterally. The spinal fluid was bloody and showed distinct xanthochromia. An encephalogram showed nothing unusual. On the third day of her stay in the hospital the patient suddenly became comatose, presented left hemiplegia and died without having regained consciousness. At autopsy the dura was observed to be normal, but under pressure. The brain was congested, and there was bloody extravasation, particularly in the right sylvian fissure. The right oculomotor nerve was fusiform and enlarged for a distance of 1 cm. Before entering the cavernous sinus it became normal again. There was a blood clot along the pons and in the interpeduncular space. The vessels were sclerotic, but no aneurysms or tears could be seen. A fresh hemorrhage, the size of a hen's egg, occupied the right frontoparietal junction. Microscopically, the hemorrhage in the third nerve was found to be central and entirely within the nerve sheath. It showed definite organization. An anomalous vascular supply was suspected but could not be proved. The authors attributed the hemorrhage to (1) rupture of a sclerotic vessel, or (2) rupture of a minute vessel with congenital aneurysmal dilatation, which was further weakened by arteriosclerosis.

COMMENT

The presence of tuberculous meningitis separates Sänger's 2 cases from the one presented here. The case described by Gurdjian and Bailey, however, is almost identical with ours. The main difference is that in their case the intraneural hemorrhage did not lead to rupture of the nerve, as it did in ours. There can be no doubt that the hemorrhage started within the nerve in all instances. All authors emphasize that the nerve fibers were displaced by the central hemorrhage and that the nerve sheath was normal and well preserved. Sänger was able even to distinguish that the hemorrhage had originated at four different points within the nerve. In his case the hemorrhage extended over almost the entire intracranial course of the oculomotor nerve, while in the case of Gurdjian and Bailey and in our case the hemorrhage was limited to a portion of the nerve. The pressure of the extravasation had produced thickening of the nerve in all cases. Torsion and flattening of the nerve took place in Sänger's first case and in ours, in both of which the nerve presented an oval instead of a round cross section.

The effect of the hemorrhage on the nerve varied. In Sänger's case the bleeding was limited to the nerve itself, and no blood was found outside it. In our case the nerve had ruptured, as we assume, under the pressure of the extravasated blood. Thus, blood could enter the subarachnoid space. In fact, the bulk of the subarachnoid hemorrhage was observed around the nerve, and no other source of hemorrhage could be made out. There are, however, objections to this view. It is strange that hemorrhage from a vessel that must have been rather

small (it could not be demonstrated anatomically or microscopically) should have produced such an extensive hemorrhage. It also is surprising that the increased intraneural pressure was not sufficient to stop the bleeding, as long as the nerve sheath was intact. But the findings in our case do not admit of another explanation. In the case of Gurdjian and Bailey, however, the nerve sheath remained intact. It is a mystery how the subarachnoid and the intraneural hemorrhage could have originated from the same point. The only explanation would be that of a hemorrhage dissecting the perineurium, but evidence of such a condition was not brought forward.

The possibility must therefore be considered that the bleeding into the nerve was only part, and not the starting point, of the meningeal hemorrhage. In our case a hemorrhagic focus in the anterior lobe of the hypophysis and subependymal hemorrhages were found. In any event, there was multiple hemorrhage in both cases. The patient of Gurdjian and Bailey died of a cerebral hemorrhage. There remains the problem of from what vessel and from what cause the hemorrhage originated. The vessels of the base could not be the source in our case, as well as in that of Gurdjian and Bailey. The latter authors suspected an abnormal blood supply, but could not find anything unusual. In our case the tissues were destroyed by the hemorrhage, and, furthermore, the distal portion of the third nerve was not available for examination.

The oculomotor nerve has, according to Sänger, a very rich blood supply. It receives two arteries, of about 0.25 mm. diameter, which arise from the point where the basilar artery gives off the posterior cerebral artery. Additional tiny vessels, which come from the posterior communicating artery, enter the nerve from above. They also supply the perineurium. Other very fine vessels enter the nerve at its root. In Sänger's case the draining small veins were thrombosed. He explained the intraneural hemorrhage by the continuing rich arterial supply with the shutting off of the venous drainage at the same time. No thrombosed veins were found by Gurdjian and Bailey or by us. Vascular changes, such as are commonly observed in the so-called spontaneous subarachnoid hemorrhage, were absent in both cases.

The possible role of hypertension in the causation of such hemorrhages should be considered. Our patient had a systolic blood pressure of more than 200 mm. at the time of his second stay in the hospital, and his diastolic pressure was never below 90 mm. of mercury. His left ventricle was moderately hypertrophied, and he had albumin and casts in the urine. The nonprotein nitrogen was at the upper limit of normal. Gurdjian and Bailey did not give the blood pressure of their patient, but they stated that three sisters died of hypertension in the fourth and fifth decades of life. There would hardly be a better explanation for the cerebral hemorrhage to which the patient succumbed than to assume a pressure crisis in the course of essential hypertension. No definite proof of this, however, can be furnished. The slight inflammatory reaction around the vessels and in the soft meninges previously mentioned probably was secondary to the hemorrhage which existed for more than a month (so-called reactive meningitis). The distention of the ventricles is sufficiently accounted for by the sub-

arachnoid hemorrhage. The obstruction might have taken place in the narrow interpeduncular space (Grinker[7]).

The course of the illness in our patient was probably such that the first hemorrhage coincided with the first attack of unconsciousness. At that time blood must already have escaped into the subarachnoid space, because the fluid was found to be definitely xanthochromic. Then, apparently, the bleeding stopped, or at least diminished to a mere trickle, until another hemorrhage caused the patient's death.

On the basis of symptoms and signs, there seems to be no way of differentiating between subarachnoid hemorrhage with palsy of the third nerve due to compression and primary intraneural hemorrhage with resulting meningeal apoplexy. However, when in a case of subarachnoid hemorrhage the oculomotor nerve is involved from the beginning and exclusively, without any signs of disturbance of the other cranial nerves, one may think of the possibility of intraneural hemorrhage.

SUMMARY

1. A case is presented of spontaneous hemorrhage into the intracranial portion of the oculomotor nerve with subsequent self amputation of the nerve and resulting subarachnoid hemorrhage.

2. No other report of such self amputation due to hemorrhage could be found.

3. The literature contains the reports of 1 other case of spontaneous hemorrhage into the third nerve and of 2 such occurrences associated with tuberculous meningitis.

7. Grinker, R. R.: Neurology, ed. 2, Springfield, Ill., Charles C. Thomas, Publisher, 1937, p. 952.

Technical and Occasional Notes

A CHAIR FOR ENCEPHALOGRAPHY ADAPTED TO CHILDREN AND ADULTS

MAX T. SCHNITKER, M.D., TOLEDO, OHIO

The precise technic of carrying out an encephalographic examination has been well described by many authors and is now fairly well standardized.[1] The best procedure, obviously, is that which is the most simple and can be carried out rapidly, with assurance of the best results. Except in large institutions carrying on specialized work, the

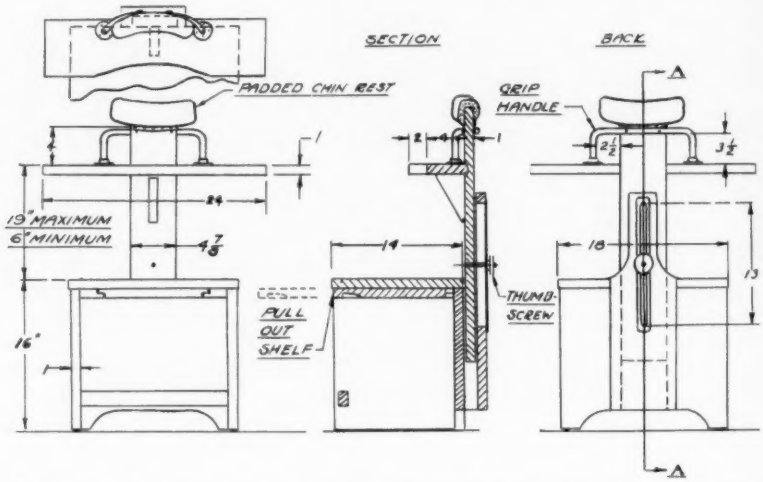


Fig. 1.—Plan of construction of a chair for encephalography. (Scale: ⅛ inch = 1 inch.) Mr. F. D. Sweeney made this drawing.

patient commonly sits on a bed or operating table, or even astride an ordinary chair, while the air for the encephalogram is injected. This is somewhat cumbersome, and even uncomfortable for the patient, since he does not have an adequate head rest or anything firm to hold on to when the headache is precipitated by the injection of air. Special chairs have been designed and described, but these are expensive to build, so that the cost is frequently prohibitive.[1b, d]

1. (*a*) Dandy, W. E.: Roentgenography of the Brain After Injection of Air into the Spinal Canal, Ann. Surg. **70**:397, 1919. (*b*) Camp, C. D., and Waggoner, R. W.: Technic of Encephalography, Arch. Neurol. & Psychiat. **25**:129 (Jan.) 1931. (*c*) Sommer, F. C.: A New Apparatus for Replacement of Cerebrospinal Fluid by Air in Encephalography and Ventriculography, ibid. **26**:1337 (Dec.) 1931. (*d*) von Storch, T. J. C.: On the Technic of Encephalography, with Special Reference to Use of Apparatus, Am. J. Roentgenol. **35**:78, 1936.

The accompanying diagram and photographs show a simple type of chair, designed particularly for encephalography. The actual cost of materials for its construction is less than $15, and it can be made by any competent carpenter. The chair is of simple box type construction, having an upright sliding T support to act as a head rest and support for the arms. The height of this support can

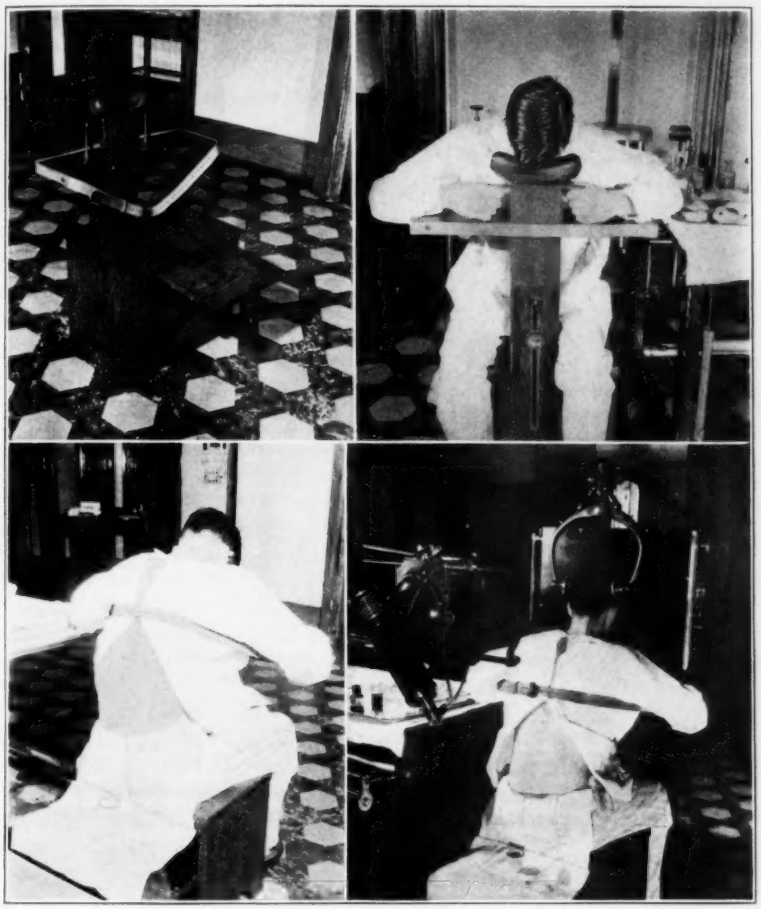


Fig. 2.—Photographs showing the chair and the steps in the encephalographic procedure.

be adjusted easily by means of a thumb screw to a proper height for small children as well as for tall adults. The head rest consists of a leather or rubber pad filled with cloth and can be kept clean easily. The head rest also acts as a support on which to rest the chin when the first roentgenogram is made, with the patient in the sitting position. Beneath the seat of the chair is a sliding panel that can be pulled out to give additional space on which to place receptacles, syringes, needles and other apparatus used in the procedure. To facilitate

moving the chair into proper position for the taking of the roentgenograms, metal flat sliding castors are provided for the chair legs. Rolling castors can be used, but they decrease the stability somewhat. The height of the chair is best set at 16 inches (40.6 cm.), as with this low seat the patient's knees are raised and the lumbar portion of the spine arched so as to facilitate the lumbar puncture. Also, small children can place their feet on the floor or a cushion and so stabilize their position.

The photographs illustrate how the procedure can easily be carried out. The patient is seated on the chair with his legs astride the upright support. A heavy leather strap is fastened around his back and is attached to both ends of the cross piece serving as an arm rest. His forehead is placed on the head rest, and he can now be given a general anesthetic (preferable for children) or a local injection of procaine hydrochloride (preferable for adults). The most convenient attire is pajama pants and reversed bed jacket commonly used in hospitals. The lower part of the back is uncovered, properly cleansed and draped. The sliding panel is then pulled out and draped with a double sterile towel, and the sterile instruments are placed on it. With the use of suitable anesthesia, one or two lumbar puncture needles are then inserted at the proper sites (depending on the technic used) and the removal of fluid and injection of air or oxygen begun. During this exchange the patient complains of severe headache, and vomiting is precipitated frequently. When this occurs a kidney-shaped basin is placed on the arm support, just beneath the chin, and the vomitus collected without any change or inconvenience to the patient or attendants. After from 30 to 50 cc. of oxygen has been injected, the patient's head is raised and his chin is placed on the head rest. The T bar is now elevated sufficiently to bring his head to an erect position. The movable roentgen grid (Bucky) is placed directly in front of the patient, his nose and forehead resting against it. A single posteroanterior roentgenogram is made, and this is developed immediately in order to determine the underlying pathologic lesion and to forestall further injection of air if any contraindication presents itself. The ventricular filling having been determined, further air can be injected (as indicated) after the head rest is lowered and the forehead placed on it as before. After the injection of air has been completed, the patient may remain on the chair and the full set of roentgenograms of the skull may be made as in the first exposure, or he may be placed flat on the roentgenographic table and the full set completed.

This type of chair has been used in a large number of cases in which encephalography was indicated. The entire procedure is carried out in the roentgenographic room. When the chair is not in use, it can be placed in an out-of-the-way corner, where it occupies little space. It is adaptable for use with children as well as adults, and the injection of air can be made with local or general anesthesia.

Obituaries

SIGMUND FREUD
1856-1939

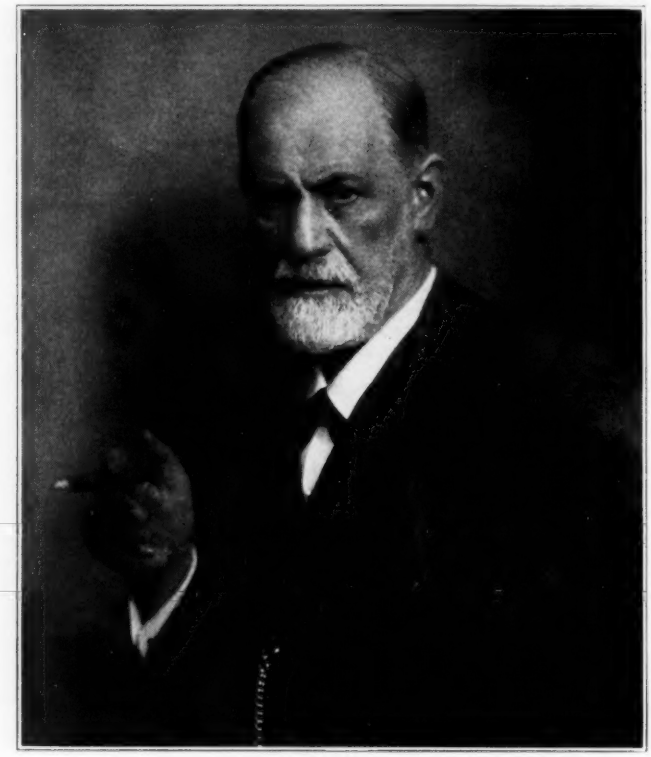
On Sept. 23, 1939, in his eighty-third year, Sigmund Freud, the founder of psychoanalysis and one of the great figures in modern medicine, died in London, England. He died in exile, away from Vienna, where he had lived for seventy-eight years and which he left when Austria ceased to be an independent state. A final evaluation of Freud's contribution will be possible only from the perspective of history, and there is little doubt that much of his concepts will undergo far reaching modifications. Even the accomplishments of the greatest genius are determined by the spirit of his time, but the earmark of a genius is that he gives more to his time than he receives from it. This was true in the case of Freud to the highest degree.

Freud for a long time was one of the most contested figures of modern times. In this respect he shared the fate of most great thinkers who introduce an original point of view contradictory to current ideas. It required nearly forty years for Freud's teachings to be recognized and assimilated by the medical profession. Today it can be said that his influence on general thought, medical philosophy and the theory and practice of psychiatry has been deeper than that of any of his contemporaries.

Freud began his medical career as a neurologist. His background was neuropathology. Two classic contributions—one on aphasia and one on infantile cerebral palsy—date back to his early medical years. Like many of his contemporaries, he soon became aware of the one-sidedness of current neurologic practice. Only Freud, unlike others, did not acquiesce so easily. Most of his patients were psychoneurotic, and the exclusively organically oriented approach of classic neurology was of no avail. As he wrote in his autobiography, in order to earn his living by giving real medical help to his patients he was looking for a different and more efficient approach. In this searching mood he went from Vienna to Charcot, in Paris, France, whose fame at that time was at its peak. From Charcot's hypnotic experiments he received the first impressions that eventually led him to the monumental intellectual accomplishments which are known today as the psychoanalytic theory and practice.

Freud's main accomplishments were to demonstrate that man's personality, normal or morbid, is shaped by life experiences; that among these experiences early childhood experiences are of overwhelming

significance and, above all, that behind a layer of civilized veneer man harbors in his unconscious mind an asocial nucleus with destructive impulses directed against others and himself. He discovered a method by which this asocial core of the personality can be explored in spite of man's natural tendency to hide it from himself and others. Freud called this tendency repression, and the method by which repressed unconscious impulses can be made conscious, psychoanalysis.



SIGMUND FREUD
1856-1939

He demonstrated that these repressed wishes and tendencies do not cease to exist even though they are excluded from consciousness. They appear in a disguised fashion in dreams; they are responsible for slips of the tongue, for the little errors which one inadvertently commits in everyday life. Moreover, they influence behavior and are the sources of many of the maladjustments which are known as neuroses and psychoses. Freud succeeded in developing a technic by which these

repressed unconscious wishes and tendencies can be brought to the surface of consciousness and thus be studied, understood and controlled by the conscious portion of the personality.

The essence of this technic is based on an extremely confidential relation between patient and physician, in which the physician assumes the role not of a judge but of a sympathetic observer. This confidential relation is the dynamic carrier of the psychoanalytic process which enables the patient to reveal his most intimate feelings and thoughts. Through his objective attitude, the physician increases the patient's courage and confidence to face his real self, which hitherto he was hiding from himself. The psychoanalytic procedure consists of a combination of two processes: (1) inviting of unconscious material into consciousness and (2) assimilation of this material by the conscious ego.

While using this method, Freud became confronted with the most intimate recesses of the emotional life. Sexual impulses played an important role in this confidential material. Nothing provoked greater consternation and rejection than the objective description of his observations concerning the role of sexual impulses in the causation of psychopathologic phenomena. Once these emotional issues had risen around Freud's observations and formulations, an objective evaluation of his findings became extremely difficult. In attacking Freud, every one defended his own repressions, the surface mask which every one wears, not only toward his fellow men but toward his own self. This emotional issue inevitably permeated scientific discussions, and Freud became the target of all kinds of accusations. He was accused of pansexualism, mysticism, dogmatism and unsound speculation. However, in his theoretic constructions sexuality did not play any greater role than in current conceptions of biology, which, like Freud, assumed two fundamental drives—the instinct for self preservation and that for race preservation. Only Freud, instead of general statements, described in detail the significance of the sexual drive in all its manifestations. The hypocritical attitude toward sex of the Victorian era is responsible for the sensational effect of Freud's statements about the importance of sexual impulses. In his later years Freud paid increasing attention to the importance of destructive hostile impulses, but these findings, although they gave a more profound view of the structure of the personality, became less publicized than his earlier discoveries.

Underlying Freud's whole approach to the understanding and effective treatment of mentally disturbed persons is the recognition of the fact that between normal and morbid the difference is only quantitative. In everyday life the behavior of a normal person is understood on the basis of psychologic causality. One considers it as an adequate causal explanation of an attack of rage when one finds that the person reacts to unjust and humiliating treatment. One readily understands

the sorrow of a person after the death of a beloved relative, or the pride and gratification which one feels after a success, or anxiety and flight in danger. Normal behavior one is able to understand in psychologic terms. Freud's main contribution to psychiatry was to demonstrate that the seemingly incomprehensible psychopathologic phenomena which do not appear as adequate responses to an actual situation can also be understood on a psychologic basis. He has shown that the same psychologic principles govern both normal psychologic reactions and the morbid reactions which one observes in mentally disturbed patients, such as seemingly unmotivated fears, depressions, doubts and elations. He demonstrated that the seeming irrationality of neurotic and psychotic behavior is mostly the result of the fact that some of the psychologic motives are not conscious. As soon as the patient becomes aware of these gaps and dares to face the conflictful motivations which he excluded from his consciousness, the neurotic and psychotic phenomena become intelligible in terms of psychology both to him and to the physician. According to Freud, psychoneuroses and many psychoses are the result of this inability of the patient to face the entirety of his emotional situation. This inability Freud considered as a failure in the highest integrative functions of the personality or, in terms of neurophysiology, of the highest integrating centers of the brain.

Freud never claimed that by understanding the meaning of the psychopathologic phenomena a universal clue to the treatment of such disturbances was found. He was fully aware of the fact that the weakness of this integrative function might be due to fundamental constitutional factors which cannot be easily changed by any form of psychotherapy. His method opened, however, the way to an etiologically oriented therapeutic approach to the emotional disturbances of a large number of patients—all of those in whom the integrative powers were relatively intact but in whom, owing to early life experiences, original impulses have been drastically repressed and eliminated from consciousness and thus removed from the integrative powers of the highest centers. Psychoanalysis is a method by which this disturbed communication between emotional life and the critical intellectual functions can be reestablished.

By his natural inclination, man is not ready to recognize the true nature of things—either in his environment or in his own self. Nothing seems to be more difficult than to see facts as they are and to overcome one's natural inclination to see things in the distorted light of one's wishes. The world outside of a person is not as he wants it to be and neither does one's own personality correspond to the picture one would like to have of oneself. Every scientific discovery means a victory of the intellect over emotionally distorted wishful thinking.

Freud takes a leading position among scientists who force man to replace self deception and superstition by recognizing the true nature of things; natural scientists are accomplishing this by exploring the world surrounding man; Freud attempted it by exploring the internal world of man himself. The history of natural sciences consists of a continuous struggle of objective knowledge against superstition and fantasy. Perhaps in no field was the battle so fierce as in the objective study of the human personality. One's own self is nearest and therefore one is least able to see it in an objective light. The picture which Freud drew of human nature was not a flattering one, and it was certainly contradictory to the common notion which people have about themselves. He has shown clearly that man is emotionally much less equipped to conduct a harmonious social life than it may seem on the surface. Under certain circumstances, when his self interest or pride is hurt, the asocial side of man becomes stimulated and his hostile and destructive impulses overtake him. Many mental disturbances are desperate defense measures of man against such impulses. Instead of becoming aware of them or expressing them directly by coordinated activity, he gives vent to these impulses in the form of uncoordinated, seemingly irrational symptoms and behavior patterns.

The secret of Freud's success lies in the simple fact that, driven by an insatiable curiosity about human nature, he patiently listened to all the details of his patients' communications and tried to discover some general principles in the chaos of the freely presented psychologic material. Disregarding the lifeless abstractions of academic psychologists who dealt only with such generalizations as will power, emotions, perceptions and apperceptions, Freud tried to understand the living person; not man in general, but the patient as an individual, with all his actual hopes, disappointments and sorrows. He made scientific use of verbal communication, by which a person conveys to another his feelings and desires and tries to make himself understood by others. Freud made a scientific instrument of the specific human faculty which every one possesses, namely, to convey thoughts and desires to others by speech. Fundamentally, psychoanalysis is the utmost and extremely refined utilization of speech for gaining insight into another person's psychologic processes.

Freud's influence on the present age cannot be fully evaluated by focusing attention on the medical implications of his teachings alone. The more precise knowledge of the development of human personality may gradually reform educational methods and lead to a systematic guidance toward mental health. The deeper knowledge of the emotional relations of man to man may be even the first step toward a more constructive social life.

Freud's contribution may be considered as the beginning of the last act of that drama of scientific development in this era, which began some four hundred years ago. First physics and chemistry made an unprecedented advance toward the control of natural forces. Simultaneously, but at a much slower rate, the development of the biologic sciences took place, leading toward a better understanding of the living organism. In this gradually unfolding pattern of scientific progress, the understanding and mastery of personality appear as the last act. Finally, after man first discovered the world surrounding him, then his own body, he is just beginning to grasp the nature of his own self. Freud was the first great pioneer of this new venture of man.

FRANZ ALEXANDER, M.D.

Abstracts from Current Literature

Anatomy and Embryology

THE EPITHELIAL COMPONENTS OF THE TELEOST PITUITARY GLAND AS IDENTIFIED BY A STANDARDIZED METHOD OF SELECTIVE STAINING. WALTER M. SCRUGGS, J. Morphol. **65**:187 (Sept.) 1939.

Seventeen species of fish, representing 15 genera from 11 different families, were studied. In addition to the pars nervosa, the teleost hypophysis is usually made up of three glandular parts: the pars anterior, the transitional region and the pars intermedia. The cytologic character of these parts, especially that of the pars anterior, varies greatly both in structure and staining capacity in different species. It is possible that factors such as age, sex or seasonal changes may explain much of this variation. The pars anterior has predominance of chromophobes or weakly staining acidophils, and a few weakly staining basophils. The transitional region has large, deep-staining basophils and carmine acidophils. The pars intermedia is most uniform in different species and has a predominance of faintly staining basophils. In all three glandular subdivisions of the pituitary body there is in certain instances a marked segregation of the types of cells. The author believes that at present it is unwise to attempt definitely to homologize the parts of the pituitary gland in the teleost with the well recognized regions in the higher vertebrates.

WYMAN, Boston.

THE NUCLEUS OF THE OCULOMOTOR NERVE WITH SPECIAL REFERENCE TO INNERVATION OF THE PUPIL AND FIBERS FROM THE PRETECTAL REGION. JAMES W. BENJAMIN, J. Nerv. & Ment. Dis. **89**:294 (March) 1939.

Benjamin reports on a study of the microscopic anatomy of the oculomotor nucleus in man and in the cat, together with the results of punctate stimulation of the nucleus and neighboring structures by use of the Horsley-Clark instrument in 21 cats. The experimental stimulations were followed by histologic study and verification of the area stimulated. In summarizing his results, Benjamin concludes that the Edinger-Westphal cells form an important and extensive portion of the center for pupillary constriction in the cat, but that the anterior median, small cell group of the oculomotor nucleus may also form part of the center in this animal. He also states that the caudoventrally arching fibers of the posterior commissure constitute a part of the pathway for the constrictor reflex. On the other hand, neither the large cells in the caudal third of the oculomotor nucleus of the cat nor the small cells in the central gray matter, dorsal to the caudal third of the principal oculomotor nucleus, are involved in pupillary constriction.

MACKAY, Chicago.

CEREBRAL ASSOCIATION PATHWAYS. M. A. GEREBTZOFF, J. belge de neurol. et de psychiat. **39**:205 (March) 1939.

Gerebtzoff produced lesions in the brains of rabbits and guinea pigs and studied the resulting degeneration in the interhemispheric cortical connections, the septum pellucidum, the cingulum and the tapetum by the Marchi method. His principal observations showed that the fibers composing the cingulum originate in the limbic area and the short fibers of the cingulum terminate near their origin or go to the dorsal portions of the frontal and parietal cortex, while the long fibers terminate in the hippocampus. The horizontal column of the fornix connects the primary olfactory cortex and the mamillary body with the region of the cornu ammonis. The fibers of the tapetum make up a large portion of the corpus callosum, but function mainly as posteroanterior association fibers.

DE JONG, Ann Arbor, Mich.

Physiology and Biochemistry

THE ELECTROENCEPHALOGRAM OF PSYCHOTIC PATIENTS. PAULINE A. DAVIS and HALLOWELL DAVIS, Am. J. Psychiat. **95**:1007, 1939.

Davis and Davis set out to determine whether brain waves of psychotic patients differ from the normal and whether they change in these patients with variations in the clinical phase. They studied 500 normal persons, 180 unselected psychotic patients and 52 schizophrenic patients. The individual records of both manic-depressive and schizophrenic patients fit into the normal variations for the most part. However, when the patients are considered as a group a higher incidence of abnormalities, such as an increased alpha index, is found. The authors then present evidence to the effect that age in itself does not change the electroencephalogram. However, the addition of a senile psychosis does alter it. Bursts of abnormal electrical activity can be correlated frequently with abnormal behavior, and these bursts of activity may be evaluated as evidence of such behavior, even if it was not actually noted at the time of the recording. It is the intermittent appearance of an abnormal rhythm which is characteristic of psychotic patients; i. e., their fundamental rhythm is unchanged except for sporadic bursts of abnormal activity. These bursts are similar to those observed in patients with relative anoxemia, epilepsy, sleep and organic lesions. All the patients in the group with conditions which were diagnosed as epilepsy or psychosis with cerebral arteriosclerosis were found to have abnormal tracings. The remaining abnormalities were scattered through various classifications.

FORSTER, Boston.

VIRUSES OF EQUINE AND OF ST. LOUIS ENCEPHALITIS IN RELATIONSHIP TO HUMAN INFECTIONS IN CALIFORNIA, 1937-1938. B. F. HOWITT, Am. J. Pub. Health **29**:1083 (Oct.) 1939.

Howitt reports that during the summer and autumn of 1937 physicians in California reported a number of cases of acute encephalitis, in some of which the course was stormy and in others less violent. There were 40 deaths. Most of the cases occurred in Fresno and Tulare Counties. During the same seasonal period in 1938 a similar type of disease, showing both the severe and the mild forms, was recorded. Fresno and Tulare Counties were again affected, with additional patients from Kern County. The western strain of the equine virus was recovered from the brain and the blood, respectively, in 2 cases. Both strains were shown to be immunologically and serologically similar to the virus of equine origin. Positive neutralization with the St. Louis virus was obtained in 49 (47.5 per cent) of 103 serums and with the equine virus (Br) in 32 (37 per cent) of 86 serums. Of a total of 63 apparently normal persons, contacts and non-contacts, residing in both the Bay Region and the San Joaquin Valley district, 8 had neutralizing substances for the St. Louis virus and 1 for the equine strain. With the exception of 1 with neutralizing antibodies for the St. Louis type, all of the group with positive reactions resided in the valley. Of a total of 47 persons tested for equine virus and 60 tested for the St. Louis strain from groups in both regions with a condition diagnosed as poliomyelitis, the only subjects with serums positive for either virus were residing in the San Joaquin Valley. Fourteen of 21 serums positive for the Br equine strain also gave strongly positive neutralization with the western virus of equine origin (Californian), while 4 gave weakly positive reactions. Neutralizing antibodies for the Br equine virus could be obtained as early as eight days after onset of the disease and were found in some persons one, two and even three years after recovery. The predominance of positive reactions for the St. Louis virus was among the older people, while that for the equine was among the younger. No definite relationship was noted between cases of the equine disease in horses and those in man. Swampy lands and many mosquitoes were closely associated with the districts affected. From the epidemiologic evidence, it seems likely that the equine virus was transmitted to man through some vector. The St. Louis strain was brought in by the migrant labor population.

J. A. M. A.

THE CORTICAL ALPHA RHYTHM IN THYROID DISORDERS. D. A. ROSS and R. S. SCHWAB, Endocrinology **25**:75 (July) 1939.

Ross and Schwab studied the cortical alpha rhythm in cases of hyperthyroidism before and after iodinization and thyroidectomy, and also in cases of patients with hypothyroidism during the course of substitution therapy. Eighty values for the alpha rate in the cortical electroencephalograms of 12 patients with myxedema and 22 patients with hyperthyroidism were compared with the basal metabolic rates. A good correlation was found to exist in the whole group, suggesting a correlation of the alpha rate and the metabolic state of the individual patient. When the alpha rhythm is taken during a "basal state" the correlation is not as good as when the patient is well fed, satisfied and relaxed. It is suggested that when low or high alpha rhythms are encountered, the basal metabolism should be measured.

PALMER, Philadelphia.

A RELATIONSHIP BETWEEN THE NATURE OF THE VITAMIN B COMPLEX SUPPLEMENT AND THE ABILITY OF HOMOCYSTINE TO REPLACE METHIONINE IN THE DIET. V. DU VIGNEAUD, H. M. DYER and M. W. KIES, J. Biol. Chem. **130**: 325, 1939.

It has been shown by du Vigneaud, Dyer and Kies that homocystine or homocysteine is incapable of supporting growth of animals on an amino acid diet devoid of methionine and cystine, supplemented daily with 0.02 mg. of crystalline thiamin chloride, 0.02 mg. of riboflavin and 0.02 mg. of nicotinic acid, with 25 mg. of ryzamin-B (an aqueous-acetone extract of rice polishings) as a source of the other vitamin B factors. With the same basal diet but with the vitamin B factors supplied by tikitiki and milk vitamin concentrate, homocystine was found to support growth. Thus, evidence has been obtained of the presence of some factor or factors present in tikitiki and milk vitamin concentrate which is not present in sufficient amounts, or is lacking, in the vitamin mixture of thiamin, riboflavin, nicotinic acid and ryzamin-B and which makes possible the utilization of homocystine by animals on a methionine-deficient diet.

PAGE, Indianapolis.

THE PHYSIOLOGY OF COLOR CHANGE IN FISHES. CLINTON M. OSBORN, J. Exper. Zoöl. **81**:479 (Aug.) 1939.

Experiments were made on the winter flounder (Pseudopleuronectes americanus), the summer flounder (Paralichthys dentatus) and the sand dab (Lophopsetta maculata). These species adapt markedly to black or white illuminated backgrounds. Exciting stimuli produce pallor and white spots in black-adapted fish, but darkening and black spots in white-adapted fish. The "excitement pallor" can be duplicated by injections of epinephrine. Results of studies of fish with denervated areas of the skin showed that the relatively rapid "general background" and "spotting" responses are independently controlled by nerves. These nervous reactions are supplemented by an "epinephrine-like" substance to produce paling and "excitement pallor" and may be supplemented by some non-nervous material to produce "excitement darkening" in white-adapted fish. A melanophore-dispersing substance from the flounder's pituitary gland might assist natural darkening in undisturbed pale fish.

WYMAN, Boston.

BLOOD PRESSURE CHANGES FOLLOWING INSULIN SHOCK TREATMENT. JOSEPH PESSIN, J. Nerv. & Ment. Dis. **90**:180 (Aug.) 1939.

Pessin observed a moderate rise in systolic blood pressure (8 to 37 mm. of mercury) and a less striking increase in diastolic pressure (5 to 13 mm. of mercury) in patients during insulin shock. These changes appeared from one to two hours after the administration of insulin, and persisted or gradually declined throughout the period of coma.

MACKAY, Chicago.

INCREASED SPONTANEOUS ACTIVITY AND FOOD INTAKE PRODUCED IN RATS BY REMOVAL OF THE FRONTAL POLES OF THE BRAIN. C. P. RICHTER and C. D. HAWKES, J. Neurol. & Psychiat. **2**:231 (July) 1939.

By means of activity drums and cyclometers, Richter and Hawkes made a quantitative study of the effects on spontaneous activity of rats of removal of the frontal pole of the brain, including the tip of the striatum. Two groups of animals were selected, one of which showed much less activity and the other much more activity than the normal average. The authors found that both unilateral and bilateral lesions increased activity. In the inactive group spontaneous activity was increased, but not to the degree of hyperactivity. In the active group, especially after removal of both frontal poles, a condition of definite hyperactivity was produced. Accompanying the hyperactivity they noted increased distractibility and irritability, the picture resembling the manic condition seen in man. The lesions were also found to increase food intake, and to decrease body weight, but there was no effect on the intake of water. Autopsy showed the ovaries to be increased and the pituitary to be decreased in weight, but the sexual activity of the animals was not tested. The authors suggest that the mechanism involved may be through removal of inhibitory influences, release of energies or increased secretory activity of the gonads. N. MALAMUD, Ann Arbor, Mich.

VITAMINS AND THE NERVOUS SYSTEM. A. AUSTREGESILO, Confinia neurol. **2**:185, 1939.

Austregesilo discusses the direct and indirect relationships of vitamins, hormones and the vegetative nervous system, particularly the role of the vitamins in nervous and psychic disorders. In both beriberi and experimental B_1 avitaminosis he found involvement of the central as well as of the peripheral nervous system, with neuronophagia in the cerebral cortex. Vitamin B complex, particularly the B_1 factor, and vitamin C are closely related to the dynamics of the nervous system, and the author has observed polyneuritis in patients with scurvy similar to that observed in patients with deficiency of vitamin B_1.

DE JONG, Ann Arbor, Mich.

THE REACTION OF THE CEREBRAL VESSELS TO INTRACAROTID INJECTION OF HORSE SERUM IN SENSITIZED AND NONSENSITIZED GUINEA PIGS. A. BUERMANN and L. ALEXANDER, Confinia neurol. **2**:215, 1939.

The vascular reaction in local anaphylactic lesions produced by intracerebral reinjection of antigen in guinea pigs is characteristically a capillary anemia. In generalized anaphylaxis, however, the expected vasoconstriction is not usually demonstrable in the pial vessels. Buermann and Alexander, therefore, tried the intracarotid reinjection of antigen to demonstrate the specific anaphylactic reaction of the cerebral vascular bed. In sensitized guinea pigs, apart from anaphylactic shock, they observed homolateral constriction of the cerebral vascular bed, including the capillaries. DE JONG, Ann Arbor, Mich.

EFFECT OF METRAZOL CONVULSIONS ON THE CEREBROSPINAL FLUID. M. SPIEGEL-ADOLF and HERBERT FREED, Confinia neurol. **2**:228, 1939.

Spiegel-Adolf and Freed made determinations of the nonelectrolyte-electrolyte ratio by a combined conductivity and interferometry method on 101 samples of cerebrospinal fluid from 46 patients with schizophrenia before and after treatment with metrazol. They found that the ratio averaged 0.26 for 35 untreated schizophrenic patients; for persons without organic disease of the nervous system the ratio was 0.22, and for patients with organic disease of the nervous system, exclusive of tumors of the brain and convulsive disorders, it was 0.30. After the first induced convulsion 60 per cent, and after repeated convulsions 82 per cent,

of the patients showed an increase in the ratio, with an average of 0.32. This corresponds to the average values for patients with epilepsy. The authors believe that this change in the ratio is the result of an increase of the tissue cleavage products in the cerebrospinal fluid, which in turn is secondary to changes in the cellular and vascular permeability. DE JONG, Ann Arbor, Mich.

ROLE OF NERVOUS STIMULATION IN THE MECHANISM OF DEVELOPMENT OF RABIES. I. A. PIGALEV, Arkh. biol. naouk **53**:52, 1939.

This experimental study was undertaken to ascertain the role played by stimulation of the peripheral nerves in the development of various trophic disturbances, not only in the region of stimulation but also in the brain. For this purpose, from 0.2 to 0.3 cc. of dilute solution of formaldehyde U. S. P. (1:50) was injected in the exposed left sciatic nerve of a rabbit. The nerve was then sectioned, the central stump sutured to the muscle and the wound ligated. Immediately thereafter, 0.3 cc. of a 2 per cent emulsion of the *virus fixé* (rabies) was injected in the subarachnoid space. The rabbit was killed on the third day, before the development of symptoms of rabies. Pieces were then excised from the cortex of each cerebral hemisphere and 2 per cent emulsions prepared from this material. These emulsions were later injected into the subarachnoid space of normal rabbits. The rabbits given injections of the emulsions prepared from the left cortex were affected with rabies, while those given injections of the material from the right cortex remained immune or had an incubation period of from six to twelve days, instead of the usual four days.

In another series of experiments, tetanus toxin was injected into the limb of a rabbit in a dose sufficient to produce local tetanus on the third day. At the same time the *virus fixé* (rabies) was injected in the subarachnoid space. The animal was killed on the third day, and emulsions were prepared from the pieces obtained from the cortex of each hemisphere. The emulsions were injected into normal rabbits. Pigalev found that rabbits receiving injections of the emulsion prepared from the ipsilateral cortex succumbed to rabies, whereas those treated with emulsion from the contralateral cortex were either immune or showed a prolonged period of incubation.

Pigalev draws the conclusion that stimulation at the peripheral end produces changes in the cerebral cortex and that a biologic stimulus, the *virus fixé* injected in the subarachnoid space meets with different conditions in the two hemispheres, conditions which will determine the further reactions. According to Pigalev, this is the reason for the dissimilarity in the virus content and virulence of the cortex of the two hemispheres of the same animal. While one hemisphere may be entirely free of the virus the other has sufficient to release all the symptoms of the disease. Pigalev claims that the virus itself undergoes biologic changes under the influence of the peripheral stimulation, as witnessed by the lengthening of the incubation period. NOTKIN, Poughkeepsie, N. Y.

THE PROBLEM OF EXPERIMENTAL NEUROSES. S. D. KAMINSKY, Arkh. biol. naouk **53**:69, 1939.

This investigation deals with the problem of active adaptation of unstable apes to experimental tests by which neuroses are induced. Kaminsky attempted to induce experimental neuroses in 3 unstable apes, with the aid of a motor-food method which usually produces neuroses in unstable dogs. Two of the experimental animals were excitable, and 1 was inhibited. One of the tests consisted of overexcitation of the inhibitory process, and the other of a collision of stimulation with inhibition and "inversion." These tests caused no disturbance in the conditioned reflex activity in the 3 animals. Kaminsky explains his results by the theory of the relatively greater liveliness of the nervous reactions in apes and by the fact that food reenforcement in apes does not reach the same degree of tension as in dogs, probably because of the higher developed reaction of orientation in apes. NOTKIN, Poughkeepsie, N. Y.

Neuropathology

ACUTE PUERPERAL HYPOPHYSEAL NECROSIS. CLARK E. BROWN and LAWRENCE F. EDER, Am. J. M. Sc. **198**:166 (Aug.) 1939.

Brown and Eder report the case of a married white woman aged 43, a primipara, in whom there developed acute necrosis of the anterior lobe of the hypophysis. Six weeks before term the blood pressure was 159 systolic and 92 diastolic; on the day of admission to the hospital it was 184 systolic and 108 diastolic, and the reaction of the urine for albumin was 2 plus. The patient was delivered of a healthy baby. The placenta could not be expressed. On the third day post partum, in spite of intravenous injection of fluids (dextrose, saline and blood) and ephedrine, the systolic pressure stayed below 90 mm.; the patient died ninety-three hours after delivery. Postmortem examination showed that many of the distended cavernous vessels of the endometrium of the uterus were filled with red thrombi. In the pars anterior of the pituitary gland all the cells stained poorly and were blurred; necrobiosis had progressed to the stage at which cell identification was difficult. The alveolar structure of the hypophysis was lost. The appearance of the gland was one of infarction. The concept of thrombosis, rather than embolism, of the vascular channels in the gland is favored. The condition described may be a more common puerperal complication than is usually recognized; hence the authors state that if the puerperal course of a patient progresses unfavorably, without obvious cause, studies of the blood sugar, active dextrose therapy and anterior pituitary extracts may be indicated.

MICHAELS, Boston.

CEREBRAL CORTICAL CALCIFICATION SIMULATING PICK'S DISEASE. EUGENE KAHN, ERNEST LION and HARRY ZIMMERMAN, Am. J. Psychiat. **95**:1027, 1939.

The authors report the case of a white man aged 56 who showed impaired business ability at the age of 37, hesitation and explosiveness of speech at 45, forgetfulness at 46 and progressive personality changes after the age of 52. His attention and concentration were poor; he was reticent, shut in and given to trancelike states, and had hyperkinesis and periods of uncontrollable laughter, indifference and lack of insight. Sleep reversal, Witzelsucht, poverty of thought and perseveration were present. Physical and neurologic examinations gave essentially negative results except for the hyperkinesis and clumsiness. Laboratory findings were within normal limits except for a slight decrease in calcium in the serum and spinal fluid, with increase in phosphorus. Roentgenograms of the skull showed extensive calcification of the temporal and frontal lobes. Air studies showed dilation of the ventricles and sulci. Examination of a biopsy specimen revealed deposits of calcium in the cortex, with decrease of cellular elements, mild glial proliferation and deposits of iron along the capillaries.

FORSTER, Boston.

CELL MINERALS IN AMAUROTIC IDIOCY, TUBEROUS SCLEROSIS AND RELATED CONDITIONS, STUDIED BY MICROINCINERATION AND SPECTROSCOPY. LEO ALEXANDER and ABRAHAM MYERSON, Am. J. Psychiat. **96**:77, 1939.

Alexander and Myerson studied 3 cases of amaurotic idiocy by microincineration and found a decrease of heat-resistant mineral ash in the cytoplasm of diseased ganglion cells with a normal amount in the cell membrane. The diseased ganglion cells showed dense aggregations of ash residue. Glial proliferation, when it occurred, gave rise to hypermineralization. Spectroscopic examination in these cases showed diminution of calcium and phosphorus. On studying 2 cases of tuberous sclerosis by microincineration, the authors found an excess of heat-resistant ash in the diseased ganglion cells, with nuclei free from these substances. Abnormal glia cells were hypermineralized. Spectroscopic examination in these

cases showed an increase in calcium. In 3 cases of spongioblastomatous periventricular hematoma also studied by microincineration, the authors found rich deposits of heat-resistant ash in the nuclei and somewhat less in the cell bodies and their processes. In 4 cases of mongolian idiocy, microincineration revealed no change.

FORSTER, Boston.

PATHOLOGIC CONSIDERATIONS ON INSULIN TREATMENT OF SCHIZOPHRENIA. ARMANDO FERRARO and GEORGE A. JERVIS, Am. J. Psychiat. **96**:103, 1939.

Ferraro and Jervis divide the histologic changes following insulin treatment into those affecting the nerve cells and those involving the blood vessels. They observed that the majority of the nerve cells appear altered and that the normal architecture of the cortex is disturbed, the neurons dropping out either diffusely or in areas. They observed also areas of proliferation of small vessels and capillaries, with proliferation of endothelial and adventitial cells. The authors assume that the changes in the nerve cells are the result of anoxia, which in turn is dependent on both the biochemical factors and the vascular changes.

FORSTER, Boston.

CEREBRAL LESIONS DUE TO VASOMOTOR DISTURBANCES FOLLOWING BRAIN TRAUMA. MAX HELFAND, J. Nerv. & Ment. Dis. **90**:157 (Aug.) 1939.

Helfand describes the histopathologic changes in the brain in 22 cases of fatal injury to the head. Cases in which convulsions had occurred were excluded in order not to confuse the interpretation of the lesions. The series included cases of bullet wounds, motor and train accidents and falls. The significant changes consisted of microscopic areas of ischemic necrosis in the cerebral cortex, the basal gray masses, the hippocampus and the cerebellum, which were distant from the gross lesions due to actual trauma. In these areas the intercellular substance stained poorly; the ganglion cells were pale, with triangular, pyknotic nuclei and absence of processes or prolonged homogeneous projections, and the vessels were dilated or collapsed and showed degeneration of the walls and diapedesis of leukocytes. In the bordering, transitional zone there were progressive astrocytic changes and neuronophagia. Compound granular cells were seen only in severely damaged areas, and in these regions mesenchymal reparative activity had led to vascular proliferation and fibrosis.

Helfand attributes this process of anemic necrosis to vasomotor disturbances which are themselves reversible, but which lead to the death of tissue and only secondarily to the death of the vascular wall. He apparently ascribes the vasomotor disturbances to the mechanical effect of the blow.

MACKAY, Chicago.

A CASE OF UNILATERAL TORSION DYSTONIA. R. GORDIN, J. Nerv. & Ment. Dis. **90**:344 (Sept.) 1939.

Gordin records the case of a man aged 23 who, shortly after a chill and fever lasting one day, began to present progressive torsion dystonia, which was limited to the left side. The face, neck, trunk and extremities were involved, with grimacing, torticollis, opisthotonos, dextrorotation of the trunk and strong inversion and extension of both left extremities. At first the movements were slight and could be voluntarily controlled; later they were massive and constant, were aggravated by voluntary activity or efforts at control and were sufficient to prevent sleep. There were no definite reflex or sensory abnormalities, and the cerebrospinal fluid was normal. During eleven days of narcosis and for several days aftrward spasms were absent, but they eventually returned. The patient died after cervical root section. Pathologic changes were observed only in the

right caudate and lenticular nuclei. In the caudate nucleus there was only slight rarefaction of the large ganglion cells, but in the putamen and in the lateral segment of the pallidum there were destruction of the large ganglion cells, neuronophagia, formation of glia rosettes and vascular proliferation. Occasional perivascular infiltrations of round cells were seen, especially in the anterior commissure near the putamen. Other parts of the brain, including the corpus luysi, the nucleus paraventricularis and the nuclei of the tuber cinereum, as well as the entire cortex, were intact. Gordin emphasizes that the encephalitic process was restricted largely to the neostriatum and affected chiefly the large cells.

MACKAY, Chicago

A DEATH ASSOCIATED WITH METRAZOL THERAPY. RALPH M. FELLOWS and FRANK KOENIG, J. Nerv. & Ment. Dis. **90**:358 (Sept.) 1939.

Fellows and Koenig report the case of a white woman aged 33 who had had a catatonic type of schizophrenia for over ten years. After eleven injections of from 3 to 5 cc. of a 10 per cent solution of metrazol she had experienced nine grand mal seizures, with considerable clinical improvement. The twelfth injection (5 cc.) was followed by wild excitement for a few minutes, but no seizure. She appeared normal thereafter. Seven and one-half hours after the injection, and immediately after eating her evening meal in an apparently normal condition, she was discovered dead in bed. Autopsy revealed pulmonary congestion, slight swelling of the liver and kidneys and a few petechial hemorrhages in the striate region of the occipital lobes. Microscopically, there was engorgement of the pial blood vessels. The perivascular spaces were dilated throughout the brain. Patchy areas were observed in the cortex in which the ganglion cells were swollen and contained granular cytoplasm and obscure nuclei. In the basal ganglia the nerve cells were pale and indistinct, with faintly staining or no nuclei, while some of the cells were swollen and distorted. The parenchymal cells in the peripheral portions of the lobules of the liver were vacuolated and granular. The nuclei had disappeared in some cells; in others they were swollen. The renal glomeruli were congested, and the spaces of Bowman contained an amorphous granular transudate. The tubular epithelium was swollen; the cells were granular and their nuclei indistinct. All other parts of the body appeared grossly and microscopically to be normal.

MACKAY, Chicago.

A CASE OF PELLAGRA: THE PATHOLOGICAL CHANGES IN THE SPINAL CORD. J. G. GREENFIELD and J. MACDONALD HOLMES, Brit. M. J. **1**:815 (April 22) 1939.

Pellagra is a rare disease in Great Britain, as indicated by the fact that only 131 cases had been reported up to 1934. In only a few of these cases did the disease occur in children. Greenfield and Holmes reported a case of pellagra in a boy aged 5 years. The treatment consisted of brewers' yeast, hydrochloric acid and an extract of fresh liver (Campolon). After two weeks there was slight improvement in the dermatologic and neurologic symptoms. At this point, the child contracted measles. He died two days later of bilateral bronchopneumonia. The only histologic observation was degeneration of neurons in the brain and spinal cord. The basal ganglia and motor cortex were extensively involved. In other parts of the cortex the destruction was less intense. None of the changes characterizing subacute combined degeneration of the spinal cord were found. The authors suggest that pellagra may be due to the deficiency of an extrinsic factor in the diet (nicotinic acid) or to failure to assimilate this factor.

ECHOLS, New Orleans.

TUBEROUS SCLEROSIS OF MALIGNANT TYPE. L. MARCHAND, M. BRISSOT and J. MAILLEFER, Encéphale **1**:57, 1939.

The authors describe a case of a malignant type of tuberous sclerosis in a 6 year old male idiot with epilepsy. The mother and both maternal grandparents were mentally deficient. A 4 year old brother was markedly retarded and epileptic and had adenoma sebaceum of the face. The patient had numerous tumors of the face, forehead and scalp and two small tumors on the trunk. He died after rapidly progressive cachexia. A few days before death, a soft subcutaneous tumor appeared in the cervical region. Both cerebral hemispheres contained multiple cortical patches of tuberous sclerosis. The walls of both lateral ventricles consisted of a soft whitish tissue, containing small hemorrhages. In the left hemisphere the choroid plexus contained numerous miliary nodules. The caudal portion of the right thalamus contained a tumor the size of a nut. The brain stem and cerebellum showed no gross lesions. The heart contained multiple whitish masses in the myocardium; there were multiple renal tumors. Microscopically, the cerebral cortex, in addition to the tubers, presented gliosis, demyelination and monstrous ganglion cells and astrocytes. The ganglion cells were few and atypically formed and contained sparse neurofibrils. The subependymal tissue showed diffuse proliferation of glia cells, many of which were monstrous and multinucleated. The thalamus contained an astrocytoma with large fusiform cells. In the right restiform body was a small nodule of cytoplasmic glia. The tumor of the choroid plexus was a meningioma made up of fusiform cells, between which were collagen and thin-walled capillaries. In the deepest portion of the molecular layer of the cerebellum were multiple small gliomatous nodules made up of astrocytes with few fibrils. The tumor of the neck was identical in structure with the astrocytoma of the thalamus. There were gigantic, polymorphous stellate cells, often arranged about blood vessels. The renal tumors were made up of granular cells in a network of reticulin. They had some features of the epithelial type of meningioma and of peripheral glioma. The myocardial tumors resembled rhabdomyoma, but contained cells of sympathoblastic type. These tumors, while they correspond to the features of rhabdomyoma, seem to be of sympathetic, and not of muscular, origin. The tumors of the skin were composed of fibroblasts, believed to be altered Schwann cells, and contained excessive collagen in the cutis. Tuberous sclerosis comprises two types of processes: (1) a diffuse growth of neuroglia cells without compression or destruction of other elements and (2) well defined gliomas, which have a malignant evolution. All these particulars indicate the close relationship between neurofibromatosis and tuberous sclerosis, both neuroectodermal, hereditary diseases, in which hyperplastic and neoplastic gliomatous lesions of the brain are observed. There are cases in which, even after histologic study, it is difficult to determine whether one is dealing with one or the other of these diseases.

LIBER, New York.

ALZHEIMER'S DISEASE WITH PICK'S ATROPHY OF THE FRONTAL LOBE. M. LIEBERS, Arch. f. Psychiat. **109**:363 (Feb.) 1939.

Liebers reports the case of a woman aged 61 who for six years showed gradual development of mental disease characterized by deterioration, memory disturbances, restlessness, occasional fainting spells and vague hallucinatory disturbances. She remained in the hospital for about three years, with gradual increase in the general deterioration, marked restlessness and some difficulty in speech but no logoklonia. There were no definite neurologic signs. Autopsy showed pronounced atrophy of both frontal lobes and of the second and third left temporal convolutions. Microscopic examination showed changes characteristic of Alzheimer's disease, with numerous senile plaques and fibrillary changes. These were pronounced in the atrophic regions, but were also scattered throughout the brain. The clinical picture and macroscopic observations seemed to be most

closely related to Pick's lobar atrophy, whereas the microscopic picture was that of Alzheimer's disease. It is pointed out that in a number of cases a condition diagnosed as Pick's disease on the basis of the clinical picture and gross appearance of the brain may on histologic examination prove to be Alzheimer's disease.

MALAMUD, Worcester, Mass.

OLIVOPONTOCEREBELLAR ATROPHY. E. WELTE, Arch. f. Psychiat. **109**:649 (April) 1939.

Welte reports 4 cases, in 3 of which there was systematic atrophy of the olivopontocerebellar system. In the fourth case the dentate nucleus–brachium conjunctivum system was affected. The two types of atrophy described in this contribution belong in the group usually classified under the generic term of spinopontocerebellar degenerations. Four subgroups are recognized: (1) Friedreich's disease, (2) olivopontocerebellar atrophy, (3) primary cerebellar atrophy and (4) atrophy of the dentate nucleus and brachium conjunctivum. The atrophy in these cases is found mainly in the periphery of the neuron, affecting mostly the white matter and only secondarily the cerebellar cortex. In the first 3 cases reported by Welte, there was additional involvement of the arcuate and pterygoid nuclei. In the fourth case, that of disturbance of the dentate nucleus, there was also a marked degree of atrophy in the spinal portions of the peripheral motor neuron system, with degeneration of the tracts in the spinal cord but also involvement of the olivopontocerebellar system.

MALAMUD, Worcester, Mass.

ASTROCYTOMA OF THE MEDULLA OBLONGATA, PONS AND PEDUNCLE. O. FOERSTER and O. GAGEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **166**:497 (July) 1939.

Foerster and Gagel report 12 cases of astrocytoma of the brain stem, 7 of which were in males and 5 in females. Five of the patients were in the first decade of life; 1 was 2 years of age. There was 1 patient each in the second and the third decade; 3 were in the fourth, and 2 in the fifth decade. The average duration of illness in the 10 cases in which such information was obtained was three years and three months; the shortest period was three and one-half months, and the longest, fourteen years and two months.

The clinical picture was recorded in 10 of the cases. In 1 case the cranial nerves and long tracts were spared. The presenting symptom was frontal headache, of two years' duration. This was due to internal hydrocephalus resulting from the protrusion of the tumor into the fourth ventricle. In most of the other cases there was alternating hemiplegia, with cranial nerve involvement on one side and hemiplegia on the other. In 1 case of pontile tumor cerebellar fits were noted. Thalamic or central pain was recorded in 1 case. Nerve deafness due to unilateral involvement of the cochlear nuclei was present. Contractures of the facial muscles were seen. In 1 case the onset of the illness was with a facial tic. In 2 cases the symptom appeared soon after trauma to the head. In 1 case there was marked improvement for six and one-half years.

In 4 cases the tumors were clearly circumscribed and in 4 others infiltrating. The infiltrating tumors were encountered mainly in older patients, except in 1 case in which it occurred in a boy aged 11. There was no histologic difference between the tumors of younger and those of the older patients. The circumscribed protoplasmic astrocytomas differed in no way from similar tumors more commonly seen in the cerebral hemispheres and cerebellum. The circumscribed fibrillary astrocytomas in the brain stem, however, were more cystic than similar tumors in the basal ganglia, thalamus or cerebral hemispheres. The authors comment on the frequency of piloidal astrocytes.

SAVITSKY, New York.

Psychiatry and Psychopathology

FATAL CASES OF ACUTE MANIC-DEPRESSIVE PSYCHOSIS. CHARLES P. LARSON, Am. J. Psychiat. **95**:971, 1939.

Larson reports 14 cases of fatal manic-depressive psychosis and points out as clinical features the short prodromal period launching into a wildly delirious state, characterized by marked maniacal as well as progressive physical symptoms, the latter progressing in severity until exhaustion and circulatory collapse occurred suddenly. In 75 per cent of the cases death occurred within two weeks. In the series of 14 cases the commonest observations at autopsy were dehydration, petechial hemorrhages in the brain, pulmonary edema and evidence of circulatory collapse. The petechiae occurred chiefly in the midbrain and hypothalamus.

The author points out that laboratory, clinical and autopsy observations in these cases were similar to those of hypochloremia, such as occurs in heat shock. The hypochloremia is attributed to the decrease in chlorides as a result of the patient's overactivity and his failure to ingest food. The petechial hemorrhages are believed to be due to the hypochloremia.

Infusions of physiologic solution of sodium chloride are advocated, as well as hypertonic solutions of sodium chloride if these are not successful. Since institution of this therapy combined with chemical sedation, 9 patients have been treated, without a fatality.

FORSTER, Boston.

COURSE AND PROGNOSIS IN SCHIZOPHRENIA. WILLIAM MALAMUD and NORMAN RENDER, Am. J. Psychiat. **95**:1039, 1939.

In a group of 177 schizophrenic patients who had been followed for five or more years by staff physicians, Malamud and Render found 14 per cent of complete recoveries and 8 per cent of social remissions. They believe that a follow-up of less than five years is inadequate. The groups were considered as to sex, age, physique, personality, intelligence, somatic pathologic conditions and permeability. The more favorable factors were found among patients of the male sex, in the second or fourth decade of life, with normal or athletic physique, cyclothymic personality and a high intelligence quotient. Positive heredity, the married state, a history of previous attacks unlike the present, an acute onset, definite precipitating factors and improvement during hospitalization seemed also to be favorable. The only favorable symptoms found were confusion, positive affect and motor activity. The authors point out that these factors cannot be considered specifically important in a given case.

FORSTER, Boston.

BILATERAL FRACTURE OF THE FEMORAL NECKS CAUSED BY METRAZOL CONVULSIONS. DONALD C. SOMERS and ROBERT P. RICHARDSON, Am. J. Psychiat. **95**:1193, 1939.

Somers and Richardson report the case of a white man aged 31 who, after the administration of metrazol, had a severe convulsion lasting three minutes, after which his lower extremities were externally rotated and adducted. Roentgenograms showed fractures of the necks of both femurs.

FORSTER, Boston.

SCHIZOPHRENIC-LIKE PSYCHOSIS FOLLOWING HEAD INJURIES. L. B. SHAPIRO, Illinois M. J. **76**:250 (Sept.) 1939.

Shapiro found that in 21 of 2,000 cases of dementia praecox a relation between trauma and the onset of psychotic symptoms was shown. In 10 cases there was no evidence of injury to the brain, but the mental symptoms developed in such close time relation to a severe trauma to the head that the sequence of events cannot be disregarded. The patients all had introverted personalities and marked hereditary tainting, so that the possibility of a schizophrenic-like reaction was

present. As a result of the injury, this latent tendency became overt, and the psychosis which followed the trauma was so-called schizophrenia. The author concludes that in this group the trauma acted simply as a precipitating factor. In the other 11 cases evidence of damage to the brain was present. Confusion, dizziness and defects in memory and orientation, as well as persistent headaches with irritability, do not belong commonly in a schizophrenic-like picture. Furthermore, in 7 of these cases the prepsychotic personality was well integrated, and hereditary tainting was present in only 2 instances. The neurologic changes, the organic-like mental symptoms and the absence of any predisposing factors in the history suggest that in these cases the trauma did more than precipitate a psychotic reaction. In producing pathologic changes in the brain, the injury would seem to have contributed to the formation of the clinical picture. Although postmortem studies are as yet not available in this group, the development of a parkinsonian-like syndrome in 1 case and the evidence of hemiplegia and convulsions in another suggest localized cerebral damage. In evaluating the part that trauma plays in the schizophrenic-like picture, the personality as a whole should be considered. In all cases of so-called schizophrenia one should consider whether the psychosis is not attributable to a definite etiologic factor, such as trauma, infection or tumor. The need is for the exact evaluation of all mental symptoms, so that the cases of psychosis following trauma may be differentiated from those of the so-called schizophrenia in which no traceable etiologic factor occurs. J. A. M. A.

A Specific Motility Psychosis in Negro Alcoholics. Sam Parker, Paul Schilder and Herman Wortis, J. Nerv. & Ment. Dis. **90**:1 (July) 1939.

Parker, Schilder and Wortis describe a new syndrome in the Negro due to alcoholism and report 7 illustrative cases. In all, the clinical manifestations included severe persecutory hallucinations, frequent paranoid delusions and a variable degree of confusion, amnesia and confabulation. The mental features resembled those in alcoholic hallucinosis except for the greater amount of confusion. In addition, a unique disturbance of motility was observed, characterized by mannerisms resembling the Faxen syndrome of schizophrenia, transitory rigidities, catatonic and cataleptic states, propulsion, or more often retropulsion, grimacing and, in a majority of the cases, a tendency to turning about the long axis, which in some cases became a whirling activity. These manifestations occurred in colorful and varying combinations, often suggesting voluntary exaggeration or playfulness. The syndrome was obviously inexorable and serious, however, since 2 patients died, 1 persisted in a severe Korsakoff state and another exhibited continued deterioration. A case of a similar condition in a white man is described, and another in a Negro with schizophrenia whose use of alcohol was less marked.

The authors believe that the condition is an organic disease of the brain due to alcoholism. They point out that none of their patients had pseudopellagra. The racial factor is remarkable. Since the usual forms of alcoholic encephalopathy occur equally in Negroes and in white persons, this new condition is not typical of the encephalopathy in Negroes, but is a specific type observed only in members of that race.

Mackay, Chicago.

Theory for Cause of Deaths in Acutely Disturbed Mental Patients. W. A. Thompson, Psychiatric Quart. **13**:503 (July) 1939.

Of the 2,038 deaths that occurred at the Rockland State Hospital during a period of seven years, Thompson found 40 that were sudden and unexpected. The causes of these 40 deaths were assigned to "acute exhaustion of the insane." The author shows that these deaths are related, or possibly due, to dysfunction of the hypothalamus. The observations seem to indicate an irritative lesion of the hypothalamus. This might suggest further that the whole picture of mania (hyperexcitability) can be explained on the basis of pathologic changes in the

hypothalamus. This would indicate an organic cause of hyperexcitability, and therefore of mania. Future investigation of deaths from acute exhaustion should include detailed microscopic observation of this region of the brain. Determinations of blood sugar are recommended. The trial of ergotamine tartrate is suggested as treatment for hyperexcitability.

J. A. M. A.

Meninges and Blood Vessels

THE KORSAKOFF PSYCHOSIS IN SPONTANEOUS SUBARACHNOID HEMORRHAGE, SIDNEY TARACHOW, Am. J. Psychiat. **95**:887, 1939.

Tarachow reports 3 cases of Korsakoff's syndrome in patients with spontaneous subarachnoid hemorrhage. All the patients were females, their ages being 15, 33 and 58 years, respectively. The psychosis appeared from five days to two months after the hemorrhage and lasted from ten days to one month. After recovery the patients were somewhat hypomanic. Air studies of 2 of the patients revealed internal hydrocephalus.

FORSTER, Boston.

TRANSIENT PARALYSIS FROM POSTURAL HYPOTENSION. H. M. THOMAS JR., Bull. Johns Hopkins Hosp. **65**:329 (Oct.) 1939.

Thomas reports the case of a 65 year old man who had had innumerable attacks of transient paralysis of the right arm and leg and occasional blurring of vision of the left eye. These symptoms were reproduced by raising the patient on a tilting table from the horizontal position to an elevation of 75 degrees, at which time his blood pressure fell momentarily from 130 mm. of mercury systolic and 88 diastolic to 82 systolic and 55 diastolic or even lower. The paralysis passed in five or ten minutes, with no residuum. The author believes that this apoplexy is caused by fleeting localized cerebral ischemia, which occurs in the course of a decrease in blood pressure from postural hypotension. The degree of narrowing of the lumen of the various cerebral vessels due to arteriosclerosis determines the point at which the ischemia first produces symptoms. So sudden is the paralysis in the leg that the patient falls to the ground if he is not clinging to a chair or some other object for support. Stimulation of a hypersensitive carotid sinus may cause sudden lowering of the blood pressure, but it is suggested that in this patient the postural hypotension was associated with an insensitive reflex pressor mechanism rather than with a hypersensitive reflex depressor mechanism. The occurrence of transient dimness of vision in one eye may be explained by the calcified bodies observed in a roentgenogram of the region of the internal carotid artery, which strongly suggest advanced sclerosis of this vessel. The physiologic explanation has served in this case as a basis for treatment. Treatment designed to prevent excessive decreases in blood pressure has greatly diminished the number and severity of the attacks.

J. A. M. A.

MENINGITIS DUE TO MICROCOCCUS TETRAGENUS. M. CRISCITIELLO JR., New England J. Med. **221**:383 (Sept. 7) 1939.

Criscitiello reports a case of meningitis due to Micrococcus tetragenus, with recovery. A lumbar puncture was done, and the morphologic features, the staining reaction and the cultural characteristics of the organisms were found to be consistent with those of M. tetragenus. Ordinarily this organism is found in the nose and throat, where it is not considered to be pathogenic. Although this patient gave no history of infection of the upper part of the respiratory tract, it is likely that the organism gained entrance to the central nervous system from the right ethmoid sinus. Therefore, one should carefully examine the upper part of the respiratory tract for possible foci of infection in cases of this type. A blood culture was not made on the day of admission. Although one made seven days later was sterile,

the patient had already been taking sulfanilamide for five days. The author is of the opinion that in this type of meningitis one is not dealing with a virulent type of organism and that if the patient can be kept alive until he has manufactured enough immune bodies he will recover.

J. A. M. A.

MENINGOENCEPHALITIS ASSOCIATED WITH BANG'S DISEASE. M. KESSLER and W. MÜLLER, Arch. f. Psychiat. **109**:347 (Feb.) 1939.

Kessler and Müller report the case of a woman aged 26 who for several years had suffered with vague symptoms of generalized fatigue, apathy, headaches in the frontal region and malaise. On admission she complained of pains in the back and feet, stiffness of the neck and dizziness. There were signs of meningitis both clinically and on laboratory examination of the fluid. From her first admission, at the age of 26, until her death two years later she was in the hospital for varying periods on several occasions. The first diagnosis was serous meningitis. The cell count of the spinal fluid varied from 120 to 1,200, with lymphocytes predominating. Until shortly before the final admission the temperature was not increased, and there was leukopenia with relative lymphocytosis. Bacteriologic examinations gave negative results until shortly before death, when agglutination tests of both the blood and the spinal fluid were positive for the organism of Bang's disease (Brucella abortus). Toward the end of the illness the symptoms beecame more marked, with bladder disturbances, papilledema, psychomotor restlessness, confusion and fever. The patient died in the hospital, and autopsy showed chronic meningoencephalitis with granulomas in the kidneys characteristic of Bang's disease. The encephalitic changes were marked, with large, chronic inflammatory infiltrations, reaching at times granulomatous proportions. The authors point out that in a number of cases so-called lymphocytic meningitis may be due to this disease and that if the condition is diagnosed early it can be treated successfully by specific medication.

MALAMUD, Worcester, Mass.

Diseases of the Brain

CONVULSIVE STATES WITH EVIDENCE OF BRAIN HEMIATROPHY. LOUIS CASAMAJOR and ROBERT W. LAIDLAW, Am. J. Psychiat. **96**:165, 1939.

Casamajor and Laidlaw report 9 cases of epileptic phenomena occurring in patients below the age of 15, in which roentgenograms showed thickening of the cranial vault on the side of the disorder, with overdevelopment of the frontal and ethmoid sinuses and the air cells of the petrous pyramid. Encephalograms revealed enlargement of the lateral ventricle of the same side and displacement toward that side. In 3 cases the condition was post-traumatic; in 1 it was due to birth trauma and in 4 it was postencephalitic. Convulsions were either generalized or unilateral. Convulsions, hemiparesis on the side opposite the lesions and the roentgenographic and encephalographic evidence varied in degree. The process is progressive, and the authors believe it is due to failure of the myelin to increase; hence the changes are the result of failure of growth of the brain.

FORSTER, Boston.

AGNOSIAS AND THE BODY SCHEME. J. M. NIELSEN and C. W. SULT, Bull. Los Angeles Neurol. Soc. **4**:69 (June) 1939.

Nielsen and Sult report 5 cases of disturbance of the body scheme in which they carried out detailed clinical studies. They find that the syndrome of Gerstmann, consisting of "finger agnosia," confusion of right and left, agraphia and acalculia, may be part of general autotopagnosia and may be broken up into its elements on the basis of organic lesions. So-called finger agnosia, which includes visual agnosia for fingers, apractic loss of finger demonstration and inability to name the fingers or to recognize them by name, may itself be split up and encountered only in part

as a result of certain lesions. The term is thus inadvisable. The cases also demonstrate the following points: Visual verbal recognition may be preserved in the presence of Gerstmann's syndrome; general amnesic aphasia can be differentiated from finger aphasia; visual fields may be normal in the presence of Gerstmann's syndrome; revisualization of symbols (e. g., words) may be preserved with inability to form concepts through channels of taste, smell and touch; symbolic concepts may be aroused through hearing when other concepts are not recalled through this channel; amnesia for the minor (left) limbs may persist for as long as five years, as a result of a lesion in the right side of the brain.

MACKAY, Chicago.

GENEALOGICAL STUDIES IN HUNTINGTON'S CHOREA. THEODORE T. STONE and EUGENE I. FALSTEIN, J. Nerv. & Ment. Dis. **89**:795 (June) 1939.

Stone and Falstein reviewed 86 cases of Huntington's chorea, observed in the Illinois State Hospitals since 1900, with special attention to 52 cases in the Elgin State Hospital. A wide variety of racial groups was affected, Germans predominating, but Slavs, Scandinavians, Scotch, English, Jews and Negroes were also represented. The onset was most frequent in the fifth decade, but occurred in every decade from the second to the ninth. Males and females were almost equally affected. Certain clinical variations tended to run in families. In some the onset was early, in others late; in some mental symptoms preceded choreiform movements, in others the latter came first. "Anticipation," by which is meant the appearance of the trait at an earlier age in each generation, was observed, but was uncommon in this series, being most frequent when neuropathic stocks bred together. Of the 52 cases at the Elgin State Hospital, 35 were typical in every respect, including a positive family history. In 17 cases the hereditary factor was not evident. Stone and Falstein believe this is due to the incompleteness of their data, and that in reality the disease behaves genealogically like a mendelian dominant trait.

MACKAY, Chicago.

PROLONGED NONHYPOGLYCEMIC COMA OCCURRING DURING THE COURSE OF INSULIN SHOCK THERAPY. HERBERT FREED and EARL SAXE, J. Nerv. & Ment. Dis. **90**:216 (Aug.) 1939.

Freed and Saxe report 9 cases of nonhypoglycemic coma following therapeutic insulin shock. The syndrome consists essentially of prolonged coma, coming on after the administration of dextrose for the termination of insulin shock and lasting from twelve to seventy-two hours or more. Associated phenomena may include convulsions, fever, hyperglycemia and various neurologic signs, such as mydriasis, paresis and pathologic plantar responses, with cyanosis, hyperventilation and, terminally, circulatory failure. In 1 case subarachnoid hemorrhage occurred. The patients exhibit restlessness, defects of memory and judgment and disorientation. Silliness and echolalia may be observed. The symptoms are usually transient, though death has occurred in similar recorded cases. Freed and Saxe report depletion of chlorides in the blood, spinal fluid and gastric juice. They believe that the vegetative centers about the hypothalamus are most involved, but that the process is reversible in the majority of cases. In fatal cases hemorrhages have been found. The authors offer no therapeutic suggestion except sedation with use of barbiturates, oxygen for cyanosis and spinal puncture. The prognosis is usually good both for the immediate reaction and for the original psychosis.

MACKAY, Chicago.

ALTERNATING HEMIPARETIC MIGRAINE SYNDROME. J. B. DYNES, Brit. M. J. **2**:446 (Aug. 26) 1939.

Dynes records the cases of a mother and daughter who suffered from migraine and paralysis on the side opposite that of the headache. They usually were warned of an approaching attack by prodromes: general malaise and chilliness. The

attack itself was ushered in by numbness, tingling, marked weakness and loss of power in the arm and leg opposite that of the headache. The migraine was not always on the same side, but the paralysis was always on the side opposite the headache. Three years ago, at the age of 46, the mother was treated with radium for a uterine carcinoma. Her menses stopped. She has had no migraine headaches since and is in fairly good health at present. The daughter has noticed that a severe migrainous headache seems to be precipitated whenever her menstrual period is irregular and exceeds the usual interval of twenty-eight days. Ergotamine tartrate (0.0005 Gm.) given intramuscularly at the onset of one of her attacks altered the syndrome, as hemianopia or paralysis of the extremities did not develop. The headache, nausea, vomiting and confusion which always accompanied the attacks were not relieved. The patient is being treated with estrogenic substance in an attempt to regulate the menses and also to evaluate, if possible, the effect on the migraine syndrome. J. A. M. A.

BILATERAL SUBFRONTAL TUMOR WITH AFFECTIVE SYMPTOMS. M. DAVID and H. ASKENASY, Encéphale **1**:34, 1939.

David and Askenasy report the case of a woman aged 49 who suffered from progressive decline of vision for six months. For several years she had had repeated slight bouts of headache, chiefly nocturnal. They had become more severe one or two months before onset of the visual disturbances, after which they diminished in severity. Visual acuity was not measurable in the left eye; it was 5/10 in the right. There was bilateral atrophy of the optic disks, more marked on the left than on the right. There was failure to recognize odors bilaterally. The patient was apathetic and indifferent to her illness. She had no disturbance of speech or verbal memory. The clinical diagnosis lay between optochiasmatic arachnoiditis and direct compression of the optic nerves by a basilar meningioma. Hyposmia was in favor of the latter, which was confirmed by ventriculograms. The tumor was adherent to the right olfactory sulcus and the medial portion of the right lesser wing of the sphenoid. It passed under the falx, infiltrated the crista galli and was adherent to the medial portion of the left anterior fossa, particularly to the left olfactory sulcus. The tumor, shrunken by endothermy and carbonization, weighed 120 Gm. The patient recovered most of her vision. She was reexamined six months after the operation. Although both frontal poles had been removed, she appeared normal mentally. Tests of spatial orientation gave normal results. In the days following the operation she had visual hallucinosis consisting of indistinct images of enormous flies and birds, which seemed to increase in number and size when she looked up. She knew that they did not exist and were the effect of disease. The preoperative indifference had disappeared, but there persisted a slight loss of affective response. LIBER, New York.

POSTENCEPHALITIC DEMENTIA PRAECOX: REPORT OF A CASE. J. TITECA, J. belge de neurol. et de psychiat. **39**:417 (June) 1939.

Titeca reports the case of a man who, at the age of 20, experienced an acute febrile illness with confusion, delirium, profound prostration, incontinence and sialorrhea, but with no vomiting, extraocular palsies or meningeal signs. These manifestations subsided after about three weeks, at which time he began to show motor phenomena, with myoclonic and choreiform movements and rigidity of the trunk and extremities. After four months the general picture changed once more, and the patient presented a characteristic parkinsonian attitude, which was accompanied by typical manifestations of dementia praecox, with stereotyped gestures, periods of mutism and negativism and definite hallucinations and paranoid ideas. Titeca is of the opinion that this patient experienced simultaneously a parkinsonian syndrome and dementia praecox as sequelae of acute encephalitis.

DE JONG, Ann Arbor, Mich.

NEW CONCEPTIONS OF ESSENTIAL EPILEPSY. J. WERTHEIMER, Strasbourg méd. **99**:291 (Aug. 5) 1939.

According to Wertheimer, the term essential, or idiopathic, epilepsy does not designate a nosologic entity but is generally applied to all cases of epilepsy in which neither the clinical examination nor the history reveals exogenic factors as cause of the attacks. He concludes that essential epilepsy is a sequel of obstetric intracranial lesions, especially of intracranial hemorrhages, which may have escaped observation because their symptoms were slight. Intracranial hemorrhages are often caused by the use of forceps, that is, in extremely retarded deliveries, but they occur also as sequels of extremely rapid deliveries. Studies on the course of labor in epileptic women revealed a high incidence of the precipitate type of deliveries. Thus the infants of epileptic mothers are especially predisposed to intracranial hemorrhages and their consequences. The author shows that this circumstance may give rise to the familial and apparently "hereditary" appearance of epilepsy. However, he maintains that hereditary epilepsy in the biologic meaning of the term "hereditary" does not exist, the apparent heredity being the result of a vicious circle. After giving the clinical histories of 5 children, he stresses that, as a result of the dorsal position of the nursling, the blood discharged during the cranial hemorrhages settles in the occipital region and remains there like a foreign body until it gradually becomes organized, which may require several months. The cicatrization resulting from this process may produce epileptic attacks. The ventral position of the nursling, on the other hand, facilitates cranial circulation, favors the resorption of the sanguine effusion and thus avoids the cicatrization and the subsequent epilepsy. Placing the nursling in the ventral position is a prophylactic measure against the frequently disastrous sequels of obstetric meningoencephalic hemorrhages.

J. A. M. A.

HEREDITARY OCCURRENCE OF ALZHEIMER'S DISEASE, WITH COMMENTS ON THE PROCESS OF AGING IN THE BRAIN. E. GRÜNTHAL and O. WENGER, Monatschr. f. Psychiat. u. Neurol. **101**:8 (April) 1939.

Grünthal and Wenger report the occurrence of Alzheimer's disease in 4 members of a family. Anatomic observations were available in only 1 case, that of a man aged 62 who had been forgetful, apprehensive and irritable for two years. The patient exhibited rapid mental deterioration, with logoklonia, compulsive laughter and periods of excitement. Death occurred nineteen months after admission to the hospital. The brain showed atrophy of the frontal gyri. Microscopic examination revealed paucity of nerve cells in the second and third layers of the frontal convolutions, with an increase of neuroglia cells and a moderate number of senile plaques. Similar plaques were observed in scantier numbers in other parts of the brain, but neurofibrillar lesions of the Alzheimer type were completely lacking. A sister of the patient presented mental symptoms at the age of 56, and examination disclosed a clinical picture which closely resembled that of the patient. A history of similar mental disturbances was obtained in still another sister, who died at the age of 56, after an illness of two years' duration. The father of the patient became "childish" at the age of 60, and it was said that he displayed indications of mental deterioration before his death, which occurred a few years later.

In the opinion of Grünthal and Wenger, these observations place Alzheimer's disease in the group of hereditary disorders of the nervous system characterized by Spatz as "systematic atrophies." In addition to Alzheimer's disease, this group includes Huntington's chorea, Pick's lobar atrophy, certain atrophic diseases of the cerebellum, spinal and bulbar muscular atrophy and other diseases. Spatz expressed the belief that all these disorders are caused by premature and hereditarily conditioned aging of definite anatomic systems of the central nervous system.

According to Grünthal and Wenger, senile dementia also belongs to the hereditarily conditioned atrophic processes. They are inclined to doubt that aging of the tissues is the cause of early and excessive atrophy; it seems more likely that different conditions of a hereditary nature are able to produce a variety of chronic atrophic processes. They report the case of a woman aged 84 who showed the clinical picture of senile dementia. The brain was diminished in weight, and the lateral ventricles were dilated; yet the cerebral cortex was well preserved, and senile plaques were completely lacking. It is presumed that the diminution in size of the brain was due chiefly to loss of water from the tissues. Grünthal and Wenger suggest the possibility that the genuine, uncomplicated senile process is represented by this type of change and not by the usual alterations associated with senile dementia.

ROTHSCHILD, Foxborough, Mass.

CARBON DISULFIDE POISONING OF THE NERVOUS SYSTEM. C. BAUMANN, Ztschr. f. d. ges. Neurol. u. Psychiat. **166**:568 (July) 1939.

Baumann reports 1 case of carbon disulfide poisoning and the results of experiments on the effect of carbon disulfide on cats. The patient was a vulcanizer in a rubber factory. In February 1935, as a result of a sudden defect in the ventilating system, he inhaled a great deal of carbon disulfide gas. He felt dizzy and soon lost consciousness. He complained for some time of inordinate fatigability and perspired excessively. He was able to return to work after a few months. A few weeks later he was poisoned again by the same substance, but did not lose consciousness. He had severe frontal headaches with radiation into the temples. At the same time he conplained of sensations of cold on the right side of the body and in the back and scrotum; the right side of the body was weak. This subjective syndrome persisted until his admission to the hospital, ten weeks after the second attack of poisoning.

Objective examination showed mild bronchitis. There was delayed reaction to pain on the right side of the face, with complete anesthesia and analgesia of the right upper limb; there were similar sensory changes on the right side of the trunk, from the second rib to the costal border, with a midline delimitation; posteriorly, the sensory changes were present from the shoulder to the sacral region on the right. There was some diminution of response to pain and touch in the right lower limb; deep sensibility (position sense) was disturbed in this limb; there was some weakness of the grip of the right hand; the finger to nose and heel to knee tests revealed ataxia on the right side; dysdiadokokinesis was present on this side. The patient showed alternating manic and depressive states. At times he was overactive and overtalkative, with a tendency to be incoherent and rambling; at other times he was less active, with marked emotional lability manifested by crying spells. There were also definite memory defects. Retention was poor.

Baumann describes definite cerebellar signs on the right side in this case. The most frequent neurologic findings in the cases reported are extrapyramidal syndromes, pupillary changes and autonomic disturbances. Signs of involvement of the pyramidal tracts are unusual.

The author does not know of any anatomic studies of the nervous system in cases of carbon disulfide poisoning. He studied the effect of carbon disulfide on 2 cats. One cat died after one exposure and the other after repeated inhalations of the gas, given in an attempt to produce the picture of chronic poisoning. The internal organs showed no significant changes. There was diffuse involvement of the gray matter of the nervous system, sparing the cerebellum in the first cat only. The various stages of swelling and changes in the ganglion cells were best seen in Nissl preparations. The cerebellar changes in the second cat were limited to severe alterations of the Purkinje cells. The molecular and granular layers were not involved.

SAVITSKY, New York.

Diseases of the Spinal Cord

ACUTE (PNEUMOCOCCIC) METASTATIC SPINAL EPIDURAL ABSCESS. RUPERT B. RANEY, Bull. Los Angeles Neurol. Soc. **4**:31 (March) 1939.

The syndrome of spinal epidural abscess includes: (1) a point of origin for the infection, e. g., furunculosis; (2) root pains; (3) sphincteric disturbance and motor weakness developing a few days or weeks after the pains; (4) ascending sensory impairment; (5) subarachnoid block, and (6) fever and leukocytosis. The causative organism is most often the staphylococcus. Pneumococcic epidural abscess is rare. Raney reports 3 cases. In the first the abscess occurred simultaneously with pneumonia and was secondary to an infected submucous resection wound. The Klebs-Löffler bacillus and a hemolytic streptococcus were found in the abscess, as well as type IV pneumococcus. The patient died shortly after drainage. There were multiple abscesses in both lungs. In the second case a spinal epidural abscess (type IV pneumococcus) developed simultaneously with pneumonia in a man aged 42. Operation and drainage gave complete relief from the symptoms referable to the spinal cord, but the patient died a month later with renal and pulmonary abscesses. In the third case, an epidural abscess (type IV pneumococcus) developed secondary to pneumonia in a woman aged 57. Drainage again relieved all the spinal cord symptoms, but the patient died a month later with infections throughout the body. Raney urges the use of antipneumococcus serum in such cases.

MACKAY, Chicago.

COMPRESSION FRACTURE OF THE SPINE IN EPILEPSY. EUGENE ZISKIND and ESTHER SOMERFELD-ZISKIND, Bull. Los Angeles Neurol. Soc. **4**:45 (March) 1939.

Three cases are reported by Ziskind and Somerfeld-Ziskind in which "epileptic" seizures resulted in fractures of the vertebrae. In 1 case a man who had had convulsions for thirty-six years fell in a seizure in the bathroom and sustained a compression fracture of the second and third lumbar vertebrae. In the other 2 cases fractures of the twelfth and of the tenth and eleventh thoracic vertebrae, respectively, occurred in seizures while the patients were seated in chairs. The authors compare these cases with those in which tetanus and injections of metrazol cause fractures of the spine. Although a fall may have contributed in the first case, excessive muscular contraction seemed to be the cause in the others.

MACKAY, Chicago.

INTRASPINAL CAUSES OF LOW BACK AND SCIATIC PAIN: RESULTS IN SIXTY CONSECUTIVE LOW LUMBAR LAMINECTOMIES. F. K. BRADFORD and R. G. SPURLING, Surg., Gynec. & Obst. **69**:446 (Oct.) 1939.

In a study of 60 consecutive cases of lumbar laminectomies performed for the relief of low back and sciatic pain, Bradford and Spurling found that on the basis of the gross and microscopic observations they fell into four groups: 35 cases of herniated nucleus pulposus, 13 cases of hypertrophy of the ligamentum flavum, 3 cases of true neoplasms and 9 cases in which surgical explorations gave negative results. Disability was more apparent in the cases of herniated nucleus pulposus and hypertrophied ligamentum flavum than in the group in which no lesion was demonstrated. Pain throughout the distribution of the sciatic nerve, although at times secondary in severity to back pain, was present in 88 per cent of the cases of herniated nucleus pulposus and hypertrophied ligamentum flavum and in only 33 per cent of the cases in which explorations revealed no lesion. Therefore it seems that low back pain indicates an intraspinal lesion only when accompanied by sciatic pain. In 60 per cent of the cases of herniated nucleus pulposus there was hypesthesia or anesthesia limited to the lateral aspect of the leg or foot or both. In contrast, in the cases of hypertrophied ligamentum flavum and in those

in which no lesion was found there were areas of hypesthesia elsewhere, but in only 15 and 11 per cent, respectively, was hypesthesia limited to these areas. The immediate as well as the final result in 26 of the 35 cases of herniated nucleus pulposus was excellent. Improvement was slow in 7 cases, but there was definite relief of the more severe pain which had occurred before operation. One patient died too soon after operation to judge whether or not there was any relief, and 1 patient who was completely relieved of his pain died on the twelfth postoperative day. The longest postoperative period through which a patient has been followed is eighteen months, the shortest six months. Therefore the eventual results may not be the same as they appear at present. In the group with hypertrophied ligamentum flavum, 1 patient died of meningitis following operation. Of the surviving 12 patients, 8 recovered completely and 4 have slight residual pain, but are much improved over their preoperative state. The longest postoperative period in this group is two and one-half years, the shortest six months. Two of the 3 patients with neoplasms recovered completely and have remained well. The third continues to have mild discomfort in the region of the sacrum, presumably owing to incomplete removal of the dermoid tumor. Four of the 9 patients in whom the explorations gave negative results were relieved almost immediately by the operation, and 4 more have improved slowly. Six of the 9 patients are at present free from symptoms, 2 are moderately improved and 1 has had no modification of the severe back pain. The diagnosis of herniated nucleus pulposus or hypertrophied ligamentum flavum must be made clinically as well as roentgenologically to assure successful selection of patients for operation. The use of 2 cc. of iodized oil intraspinally is a safe procedure, and the amount is adequate for diagnosis.

J. A. M. A.

A Case of Poliomyelitis with Bilateral Paralysis of Masticatory Muscles. O. Sittig and J. Urban, Lancet **1**:865 (April 15) 1939.

Sittig and Urban report the case of a boy aged 15 who became ill with headache, vomiting, anorexia, listlessness and a temperature of 104 F. Two days later there developed herpes labialis and vertigo. The cerebrospinal fluid contained "numerous lymphocytes." Five days after the onset, examination revealed normal pupils, paresis of the left abducens nerve, photophobia, weakness of the right side of the face and weakness with loss of reflexes of the right upper extremity. Evidence of meningeal irritation was present; examination of the spinal fluid disclosed a positive Pandy reaction and a total protein content of 40 mg. per hundred cubic centimeters. The patient seemed to improve after the administration of 80 cc. of convalescent serum intramuscularly. Electrical tests showed that the masseter muscles were not excitable on either side, and direct stimulation produced a slow contraction of the third branch of the facial nerve. The patient had to press his lower jaw against his upper teeth with his hand in order to chew. After about six weeks the patient was discharged as improved. There was residual weakness of the right deltoid muscle. The temporal muscles were atrophic. The patient, however, could open and close his mouth. Both masseter and temporal muscles did not react to faradic stimulation; galvanic current produced only a slow contraction. This case is considered as probably one of the pontile or pontobulbar type of poliomyelitis.

Krinsky, Boston.

Encephalomyelitis Following Administration of Sulfanilamide. J. H. Fisher, Lancet **2**:301 (Aug. 5) 1939.

Fisher cites 2 cases in which symptoms of encephalomyelitis appeared after the administration of small quantities of sulfanilamide. The total doses taken were small (14 and 18 Gm., respectively), and if the drug was responsible, the patients must have been more than ordinarily susceptible to it. There is such evidence in patients suffering from certain illnesses—including acute rheumatic fever and

lupus erythematosus—in which toxic manifestations after taking sulfanilamide are especially likely to develop. Vascular changes are seen in some cases of encephalomyelitis, and their relation to the demyelinating lesions is discussed.

J. A. M. A.

TRAUMA AND PROGRESSIVE MUSCULAR ATROPHY. J. W. A. TURNER, Lancet **2**:549 (Sept. 2) 1939.

Turner says that the part played by trauma in the initiation of progressive generalized nervous diseases becomes occasionally subject to dispute in relation to workmen's compensation. In view of the lack of data derived from any notable series of cases, it seemed to him worth while to analyze a series of cases of progressive muscular atrophy to find out in what proportion a history of trauma exists. The term progressive muscular atrophy is taken to include amyotrophic lateral sclerosis and progressive bulbar palsy with muscular atrophy. The author studied a series of 100 consecutive cases. In 37 cases there existed signs of progressive degeneration of the bulbar nuclei associated with generalized muscular atrophy and fibrillation, either with or without evidence of involvement of the pyramidal tracts. In 40 cases progressive muscular wasting was associated with evidence of involvement of the pyramidal tracts. Widespread muscular wasting and fibrillation characteristic of the classic type of progressive muscular atrophy without involvement of the pyramidal tracts was observed in 19 cases. Postmortem confirmation of the diagnosis was obtained in 4 cases. For purposes of control, a second series of 100 cases of other organic nervous diseases were analyzed. This series included patients of the same age and sex suffering from various organic diseases of the nervous system in which trauma is not thought to be an etiologic factor. A table records frequency of trauma in the two groups of 100 cases. There was no history of trauma in 79 cases of the group with progressive muscular atrophy and in 78 cases of the control group. Thus, the total number of cases in which there was a history of trauma was practically identical. It was only when an arbitrary period of a year was taken that a small difference in favor of the group with progressive muscular atrophy was apparent. In 5 of the cases of progressive muscular atrophy there was a history of injury within a year of the first symptom, and in 3 of these the injury was within a month of onset. The author reports the details in these 5 cases. He reaches the conclusion that trauma has no primary part in the causation of the disease, but in a small minority of cases seems to precipitate the appearance of symptoms.

J. A. M. A.

OTITIC ZONA, ASSOCIATED WITH ZONA OF THE TRIGEMINAL GLOSSOPHARYNGEAL AND SUPERIOR LARYNGEAL NERVES. BALDENWECK and DEGORCE, Rev. d'oto-neuro-opht. **17**:29 (Jan.) 1939.

Baldenweck and Degorce report the observation of a case of otitic zona, with involvement of the right fifth, ninth and tenth cranial nerves. Both the cochlear and the vestibular division of the eighth nerve were involved. The eruption appeared on both sides of the epiglottis. The question is raised whether the upper cervical plexus was involved. Despite the fact that the eruption occurred also in the submaxillary and retroauricular regions, it is suggested that this may have been due to involvement of the cervical branch of the seventh and of the recurrent sensory branches of the fifth nerve, respectively. Furthermore, the opinion is expressed that it is more logical to believe that the seat of the lesion was in the bulbar nuclei rather than that a number of ganglia were involved. Support for this opinion is supplied by the facts that the facial paralysis was limited to the upper branch of the nerve and that the left cochlear and vestibular nerves were also affected to some degree.

DENNIS, San Diego, Calif.

Encephalography, Ventriculography, Roentgenography

A Roentgenologic Symptom of Tumors of the Posterior Fossa. Jean Rossier, Rev. neurol. **71**:289, 1939.

The normal roentgenographic appearance of the basilar plate was studied in 99 cases. Seen in profile, it is a straight or slightly and regularly curved line connecting the base of the posterior clinoid processes with the anterior margin of the foramen magnum. In 14 of 28 cases of cerebellar tumor a marked incurvation of the basilar plate, with a posterosuperior concavity, was shown. The depth of this concavity may reach 5 mm. Either the whole or only a part of the basilar plate may be curved. Of 13 cases of tumors of the acoustic nerve the incurvation was present in only 2. It was absent in 7 cases of arachnoiditis of the posterior fossa and in 46 cases of supratentorial tumors. The deformity is easy to distinguish from the sharply localized notch in the basilar plate produced by chordoma. The age of the patient, the duration and the histologic type of the tumor had no relation to the presence of the incurvation. In the cases in which it occurred, the vertical and horizontal diameters of the posterior fossa did not differ from the corresponding diameters in other cases, including those of normal subjects, suggesting that the incurvation of the basilar plate was not due to a general increase in dimensions of the posterior fossa.

Liber, New York.

Role of Arteriography in Neurosurgery. E. Mackh, Deutsche Ztschr. f. Chir. **252**:145 (June 17) 1939.

In performing arteriographic examination Mackh employs a colloidal suspension of thorium dioxide, which he injects with the aid of a record syringe armed with a cannula and without the intervention of a tubular system. Bilateral arteriography is indicated only exceptionally. Secondary arteriography is technically difficult. The method should be performed by the surgeon who undertakes the subsequent operation and who is willing to assume the responsibility for both. The author considers the method entirely harmless. The development of a tumor following the injection of thorium dioxide has not been demonstrated either in man or in animal experiments. Chemical analytic studies failed to demonstrate retention of the thorium. Fatalities developing suddenly after injection of thorium dioxide are not to be charged to the drug. The field of usefulness of arteriography is in neurosurgery, and not traumatic surgery. The method is of value in demonstrating tumors of the cerebral hemisphere. It is of no value in cases of tumors of the posterior cranial cavity and medially located tumors at the base of the cranium, such as those of the hypophysis, the suprasellar tumors, tumors of the third ventricle and craniopharyngomas. Arteriography is better tolerated than ventriculography and is to be preferred for patients in poor condition. An arteriogram is capable of furnishing a topographic and qualitative diagnosis of a tumor, and thus renders ventriculography unnecessary. The principal purpose of arteriograms is localization and recognition of the kind of tumor in the cerebral hemispheres. In the case of tumors of the temporal lobe, arteriography is indicated for the purpose of localization or when the ventricle of the involved side fails to fill in a ventriculogram. Tumors of the frontal lobe, of the temporal lobe and of the parietal and occipital regions give typical appearances of the blood vessels in arteriograms. An abnormally dilated lumen and atypical and irregular arrangement of the blood vessels suggest a malignant glioma. The diagnosis of the kind of tumor in the temporal lobe is difficult because of comparative paucity of blood vessels. Pronounced displacement of the middle cerebral artery and of the carotid stem makes it possible to diagnose a malignant glioma with this localization. Meningiomas with a parasagittal localization are recognized by the increase in the blood vessels in the corresponding portion of the falx. It is necessary here, however, to take arteriograms in two levels. The differential diagnosis of other benign tumors is largely impossible in an arteriogram. The most valuable aspect of the method is the possibility of establishing in all cases the diagnosis of a malignant glioma and thus to avoid an unnecessary operation.

J. A. M. A.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

GILBERT HORRAX, M.D., *in the Chair*

Regular Meeting, Oct. 19, 1939

The Role of the Autonomic Nervous System in Visceral Sensation. DR. JAMES C. WHITE and DR. REGINALD H. SMITHWICK.

According to strict definition, the parasympathetic and the sympathetic nerves, which arise from the brain stem and the thoracolumbar and sacral portions of the spinal cord, are purely motor in function and control homeostasis. The fact that apparently all forms of visceral pain can be relieved by sympathectomy does not fit into this concept, but it has been explained by recent findings of neurophysiologists. Their investigations have shown that afferent nerve fibers, which differ in no way from those in a sensory nerve to the skin, run in the cardiac, splanchnic and other sympathetic trunks. They differ from the classic autonomic fibers in that they have no synapses in the peripheral ganglia and they enter the spinal cord over its posterior roots. These structures may be referred to as the viscerosensory fibers, in contrast to the true autonomic or visceromotor fibers of Gaskell, Langley and Cannon.

Dr. Mixter and we have studied these structures over the past ten years in our work on the relief of intractable visceral pain. The vagus nerve, although it carries many typical afferent fibers, fortunately plays no important role in the mediation of visceral pain, which is an important function of the thoracic, lumbar and sacral nerves. Illustrations are given of the consistent relief afforded patients with angina pectoris and painful aneurysms of the aortic arch by resection or by injection of alcohol into the upper thoracic sympathetic ganglia. Experimental pain produced by distending a balloon in the upper part of the small intestine can no longer be felt after splanchnicectomy. Similarly, pain associated with ulcers penetrating the posterior duodenal wall and with carcinoma of the liver has been relieved by blocking the splanchnic rami. In cases of dysmenorrhea of uterine origin the cramplike pains disappear after resection of the superior hypogastric plexus, but in cases of carcinoma originating in either the uterus or the cervix the pain is usually due to extension into neighboring tissues and requires section of the spinothalamic tracts for relief. The same is true of pain in the bladder. Occasionally the pain of chronic interstitial cystitis can be relieved, at least in part, by presacral neurectomy. But with tuberculous cystitis, as well as with carcinoma of the bladder and of the prostate, most of the sensory impulses run over the lower sacral nerves.

We have found that certain fundamental principles govern the success of operations which are designed to denervate peripheral arteries. These principles are: 1. Any operation should be complete. 2. As far as possible the operation should interrupt the preganglionic rather than the postganglionic portion of the pathway. 3. It should be done in such a way that the possibility of future regeneration is minimized as much as possible.

Regarding the surgical treatment of hypertension, in the light of these principles it seems definite that if an adequate interruption of the splanchnic bed is performed, a definite alteration of blood pressure may be expected in every case. The nature of this effect is a lowering of the systolic and diastolic pressures and a narrowing of the pulse pressure. Immediately after operation, if it is adequately complete, a profound fall in the blood pressure level is noticed in every case as the patient

changes from the lying position to the sitting or standing position. Time alone will enable one to judge the value of adequate denervation of the splanchnic bed as a method of treatment of essential hypertension. Failure of operation in the past to cause any effect on the blood pressure level in hypertensive patients is undoubtedly due to anatomic variations and to the fact that adequate denervation did not result for this reason. The operation which we have found consistently to have a characteristic effect on the blood pressure is total removal of the great splanchnic nerve and excision of the sympathetic trunk from below the first lumbar segment to above the ninth dorsal segment through a twelfth rib exposure. This enables one to work both above and below the diaphragm, to explore adequately the kidney and adrenal glands and to exclude the possibility of paragangliomas.

DISCUSSION

DR. JAMES B. AYER: I do not feel qualified to discuss this subject, but I have followed with interest the work of Dr. Smithwick and Dr. White. It is important that they have been able to show by their studies much more of the anatomic connections of the sympathetic nervous system than was known when I studied anatomy. I wish to ask Dr. White what the present evidence is regarding the transmission in the spinal cord of painful stimuli from the viscera. In some cases chordotomy produces analgesia of the skin but the patient still complains of pain. What is the physiologic mechanism by which stimuli reach the sensorium in such cases? Is it somatic or vegetative?

DR. GILBERT HORRAX: I also feel unqualified to speak on this subject, but pain is a problem which all surgeons must deal with. I was especially interested in the ways that sympathetic pathways could be interrupted by anterior or posterior root section. In the operation described by Dr. White, I wonder if it would be a great deal more difficult to do a small laminectomy and divide the upper four roots intraspinally than to do the more extensive operation, extraspinal sympathectomy.

DR. HALE POWERS: I should like to ask Dr. Smithwick and Dr. White if it is possible to discover any pathologic changes in the ganglia themselves.

DR. WILLIAM L. HOLT: Dr. Smithwick mentioned that postganglionic sections are much more effective against the symptoms of Raynaud's disease than preganglionic sections. I wish he would explain the reason for this difference.

DR. REGINALD SMITHWICK: As far as I know, none of the ganglia which I have removed have shown any pathologic changes. No elaborate studies have been made.

In regard to preganglionic versus postganglionic sympathectomy, the work which Dr. White, Dr. Freeman and others have done on that subject (Smithwick, R. H.; Freeman, N. E., and White, J. C.: Effect of Epinephrine on the Sympathectomized Human Extremity: An Additional Cause of Failure of Operation for Raynaud's Disease, *Arch. Surg.* **29**:759 [Nov.] 1934) is probably familiar. It has been shown that in animals and human beings the body has certain compensatory mechanisms after the sympathetic pathways are completely divided. Immediately after sympathectomy, say a day after, relaxation of the vascular bed is complete. However, as time goes on the vessels regain a certain amount of tone and apparently become sensitized, so that under certain conditions, such as exposure to pain or cold and emotion, vasoconstriction of a certain degree takes place. This is not as great as when sympathetic vasomotor fibers are intact, but it may be of a considerable degree. The mechanism of this has been shown to be a humoral one, and of the substances which produce this effect epinephrine is the most important. If the preganglionic pathway is divided, vasoconstriction is only about one third as great by quantitative measure as after the resection of the postganglionic fibers. The result clinically is such, as in Raynaud's disease, for example, that if one denervates by postganglionic section a hand and by preganglionic section a foot and places the patient in a cool room, the hand will turn blue while the foot remains pink. The net result, so far as the patients are concerned, is that on exposure to pain, cold or emotion they have a recurrence

of vascular spasm to such a degree that the result of the postganglionic section is unsatisfactory and is hardly worth doing, in contrast with the result obtained from section of the preganglionic pathways.

DR. JAMES C. WHITE: In answer to Dr. Ayer's question regarding the conception of relief of visceral pain by chordotomy, I must say that one does not often have a chance to study this clinically. When pain from abdominal viscera, as exemplified by carcinoma of the stomach, bladder or uterus, becomes strong enough to require surgical intervention, it is usually no longer true visceral pain. It has spread out to the nerves in the mesenteries or in the broad ligaments or into the lumbosacral nerve plexus. Pain of this type is transmitted from the somatic nerve endings in the parietal peritoneum, and, as Morley pointed out, it is then no longer true visceral pain. This type of pain is effectively relieved by chordotomy. On the other hand, chordotomy will not relieve discomfort of an acutely distended bladder. This can readily be shown by cystometrogram. The bladder feels full and uncomfortable. I believe that sensation from stretching hollow viscera travels up the spinal cord in the posterior columns. We are now trying to find out whether this is the general rule by distending various portions of the gastrointestinal tract. In this connection, Davis and Pollock (Davis, L.; Pollock, L. J., and Stone, T. T.: Visceral Pain, *Surg., Gynec. & Obst.* **55**:418 [Oct.] 1932) have shown that in dogs if the gallbladder is distended with a balloon after previous division of the right splanchnic nerve, no pain is felt. But even bilateral chordotomy will not relieve this type of pain. I should like to ask about the results Dr. Horrax has obtained with chordotomy.

Regarding projection of visceral pain to the surface of the body, one of the most interesting books is by Morley (Morley, J.: Abdominal Pain, New York, William Wood & Company, 1931); he brings out the contribution by James Ross of Manchester, England, in 1887. Ross preceded Mackenzie by a number of years. He described two components of visceral pain: (1) the dull, boring protopathic type, poorly localized in the midline, which he called splanchnic or direct visceral pain, and (2) the more acute and better localized type, which he spoke of as "referred." Mackenzie dropped the idea of direct visceral sensation and tried to explain it all on the basis of referred pain, but he only confused the issue, without adding anything new.

DR. GILBERT HORRAX: I have had 1 case of renal crisis in which the pain was relieved by chordotomy. There were also at least 2 patients with gastric crises who were also relieved, but this condition is not a fair test, as Dr. White said.

GILBERT HORRAX, M.D., *President, in the Chair*

Regular Meeting, Nov. 16, 1939

Comparison of the Davies-Hinton and the Wassermann Reaction of the Cerebrospinal Fluid. DR. CHARLES BRENNER.

The results of 2,110 consecutive, simultaneous Davies-Hinton and Wassermann tests made in the Massachusetts State Laboratory on cerebrospinal fluids of patients in the Boston City Hospital from 1936 to 1938 were analyzed. There were agreement in the results of the two tests in 97.2 per cent of the cases and disagreement in 2.8 per cent. Cerebrospinal fluids giving a positive Wassermann reaction with less than 2 cc. always showed a positive Davies-Hinton reaction. In all but 2 of the cases in which the results disagreed the Davies-Hinton reaction was more positive than the Wassermann. No disagreement in the results was found for nonsyphilitic patients. A positive Davies-Hinton reaction was often found in syphilitic patients under treatment with no other signs of syphilis of the central nervous system, while a negative Wassermann reaction was not infrequent in patients with signs and symptoms of activity of syphilis of the central nervous

system. In patients under therapy for syphilis of the central nervous system the Davies-Hinton reaction of the cerebrospinal fluid often remained positive or doubtful after the Wassermann reaction had become negative and rarely, if ever, became negative before the Wassermann reaction.

The questions are raised (*a*) whether the occurrence of a positive or questionable Davies-Hinton reaction of the cerebrospinal fluid of a patient with no signs or symptoms of syphilis of the central nervous system is sufficient for a diagnosis of asymptomatic neurosyphilis, and (*b*) whether treatment of patients with syphilis of the central nervous system should be continued until the Davies-Hinton reaction has become negative. It is concluded that neither of these questions can be adequately answered at present, but some evidence is adduced for an affirmative answer to the second question.

DISCUSSION

Dr. John Davies: I have nothing to add to Dr. Brenner's careful, clear and impartial evaluation of this test of the cerebrospinal fluid. As a pediatrician I see little syphilis of the central nervous system. I should like to add a simple remark —like the Wassermann test, the Davies-Hinton test can easily be adapted to titration should the strength of the reaction seem important to the clinician.

Dr. H. Houston Merritt: I am pleased to hear Dr. Davies say that his modification of the Hinton test of the cerebrospinal fluid can be adapted to titration. Although one cannot use the strength of any reaction of the spinal fluid as an absolute guide in diagnosis and treatment, it is of value in certain cases. One always expects a strongly positive Wassermann reaction with even as little as 0.1 cc. of the fluid of a patient with dementia paralytica. In the regulation of treatment of any patient with a positive Wassermann reaction of the cerebrospinal fluid, there should be a gradual shift toward a negative reaction. If the reaction is positive with 0.1 cc. and gradually becomes negative with 0.1 and 0.2 cc. one knows that one is making headway. If, however, it still remains positive with 0.1 cc. intensification or change of the type of treatment is indicated. From Dr. Brenner's analysis it seems that the Davies-Hinton test is slightly more sensitive than the Wassermann. If the results can be titrated, I do not see why it is not as good, if not better, than the Wassermann test.

Dr. Henry Viets: There is a small group of cases which Dr. Brenner did not mention and which is important in demonstrating the value of the Davies-Hinton test in cases of syphilis of the nervous system. Ordinarily in treatment of neurosyphilis the first response in the cerebrospinal fluid is in the cells; this is followed by reduction in the total protein content and lowering of the colloidal gold reaction. Usually the Wassermann test is the last to respond. This is seen clearly when the intraspinal methods of treatment are used and the abnormal reactions disappear almost invariably in this order. There is, however, a small group of cases in which, for some reason, the Wassermann reaction becomes negative before the colloidal gold curve or the tests for protein show much change. This sometimes happens even before the cellular response becomes normal. It is in this group of cases that the Davies-Hinton reaction is particularly important, because it usually parallels the results of the other three tests and will continue to be positive until the reactions of the other tests become normal.

Dr. Charles Brenner: A patient who was seen in the clinic after the results of this study were compiled had had a treatment for syphilis about ten years before, when he was found to have 15 white cells per cubic millimeter of cerebrospinal fluid and a negative Davies-Hinton reaction, with a doubtful (faintly positive) Wassermann reaction. In that case the Davies-Hinton test was not as accurate as might have been expected. With respect to other cases in which the Wassermann reaction changes out of turn, as it were, the 3 cases in group 3 in which the Wassermann reaction was negative with other signs of activity still present in the spinal fluid would fall into that group, and in each of those cases, as Dr. Viets pointed out, the Davies-Hinton reaction was still positive.

Evolution of the Concept of Functional Nervous Disease. DR. A. WARREN STEARNS.

A woman had had several abdominal operations for the relief of pain. Apparently, the pathologic change was inadequate to account for the symptoms, and finally the case was diagnosed as one of neurasthenia. The social history showed that the patient had been subjected to extreme emotional stress for several years.

Study of this case led to a search of the literature to find what the attitude had been toward such situations in the past. It was possible to trace functional nervous disorders, as described clinically at present, for about twenty-five hundred years through accounts of hysteria and hypochondria. From Hippocrates to the present, cases of such disorders have apparently perplexed physicians, who have sought explanations for the symptoms in whatever theory was current or fashionable at the time. It is noteworthy that until a comparatively recent date, during a period in which physicians had only their powers of observation to depend on, these disorders were considered to be gastrointestinal in the male and uterine in the female.

Sydenham still believed these diseases to be disorders of the vital spirits, though he said emphatically that hysteria in the female and hypochondria in the male were one and the same. It had been believed previously that the uterus was a little animal which migrated throughout the body, causing many hysterical symptoms. For the next fifty years it was believed that something was circulating in the blood. George Cheyne, in his book entitled "The English Malady," insisted that something was wrong with the "guts," that what was eaten was responsible, and he set forth a theory somewhat chemical in nature.

Robert Whytt, in 1765, used the term "nervous" and spoke of the tendency to call everything that was not understood "nervous." He expressed the belief that the symptoms were due to something in the blood. Samuel Musgrave, in 1776, set forth the theory that all diseases were nervous in origin.

At the beginning of the last century a great controversy was waged in France, one group maintaining that gastralgia and enteralgia were disorders of function without an organic lesion. The opposition stated that one might as well think of a function without an organ as of a symptom without a lesion, and they used the term chronic gastritis instead of gastralgia. Dubois, in 1833, reviewed the opinions of his predecessors and called attention to the role of disorders of the passions, such as fear, rage, hate and jealousy, in functional nervous disease; he said happiness, a joy or pleasure was never a cause. Even though called nervous, however, functional disorders were still thought of in terms of gastrointestinal and uterine disease.

In 1868, George M. Beard, of New York, used the term "neurasthenia" and brought all these disorders together under a general concept of disease due to fatigue and nervous exhaustion. He was followed by Weir Mitchell, who considered such disorders as due to deficiencies in fat and blood and recommended rest as a means of repairing such deficiencies. Janet and Bernheim were beginning to regard these illnesses as psychic disorders, and for the first time a concept of psychogenesis was intimated. While this was going on, Dr. Edward Cowles, in 1891, read a paper in Boston on "Neurasthenia" and discussed the part played by autointoxication. For a few years this theory was considered plausible. Meanwhile, the use of anesthesia and asepsis had developed to a point at which surgical procedures were relatively easy and relatively safe; consequently, a great many operations were performed on neurotic patients.

In 1913, Billings expressed the theory of focal infection, and this was immediately developed to cover somewhat obscure nervous complaints. Then the theory of glandular dysfunction, or endocrine disturbance, was much in vogue for a while. At this time, the development of the theory of psychogenesis was parallel, but not identical, with the main course of medical thought. The rank and file of physicians still looked for physical disorder in cases of functional disease.

Lately, internists have been studying these conditions, and one finds Alvarez, in "Nervous Indigestion," setting forth with remarkable insight the digestive disturbances of neurotic patients. Also, from the Mayo Clinic have come other papers (Wakefield, E. G., and Mayo, C. W.: Functional or Sociologic Disorders of the Colon, *J. A. M. A.* **111**:1627 [Oct. 29] 1938. Rivers, A. B., and Mendes Ferreira, A. E.: Incidence and Causes of Chronic Dyspepsia at Various Ages, *ibid.* **110**:2132 [June 25] 1938).

This leads to a tenable hypothesis, namely, that many of these nervous disorders are visceral responses to social stress. Finally, cases are discussed in which persons with functional nervous disorders gave histories of long-standing environmental stress. A formula is set up as follows: Social stress—nervous tension—low mood—visceral response—functional nervous disease.

DISCUSSION

DR. C. MACFIE CAMPBELL: Gratitude is due to Dr. Stearns for his elegant and interesting presentation of man's pilgrimage throughout the ages. An enormous territory was covered, and it was sketched dextrously. If one considers the situation at present and looks back over the past century, perhaps there is much on which to congratulate oneself, and perhaps progress with regard to this special field of disease is not especially discouraging. One must remember that in 1821, when Georget published his book, dementia paralytica was just being defined by Bayle and Calmeil and that it was one hundred years before Noguchi and Moore demonstrated the spirochete in the parenchyma of the brain. The investigation of human nature has been complicated by residuals from the old theological superstitions of the Middle Ages and later centuries. Even in the early part of the nineteenth century Heinroth debated whether to go into medicine or theology; unfortunately, he chose medicine.

The language which is used in psychiatry is unavoidably complicated by associations and overtones, which makes it difficult to formulate observations in a clear way. Vaccines and vitamins, on the other hand, are specific terms, with regard to which there can be little misunderstanding.

Nervous disorders are disorders of the human being. When one is interested primarily in cellular pathology or is fascinated by biochemistry or bacteriology, concern with the human organism may be largely discarded. This tendency is still present, and in places even accentuated, but it has gradually come to be recognized that it is dangerous to ignore the unity of the organism and to discard personality, and to treat the patient as a structural machine or as a pharmacologic or chemical factory. At present physicians are beginning to think of human nature in a better way, not only physiologically but psychologically and anthropologically. A great debt is owing to the anthropologists.

There is available now a body of knowledge with regard to the adaptative mechanisms of the organism. It is important to bring these factors together during the next period and to replace antagonistic formulas with a wholesome synthesis. One must do justice to man's physiologic systems as well as to his complex functions as a human being, and one must recognize the environment in which he lives, which is saturated with value. If the physician disregards these factors he neglects the patient and may be led into polysurgery or polypharmacy.

DR. HENRY VIETS: I, too, wish to tell Dr. Stearns how much I enjoyed his splendid summary. One turns over in one's mind the speculative theories of Hippocrates and Galen and the beginning of the experimental method of investigation, which started with Whytt in 1750. He was the first to apply this method in the sense in which it was used by Harvey, more than one hundred years before. The ideas of Whytt continued up to the time of Claude Bernard, who emphasized the effect of environment on the internal mechanism of man and paved the way for the most important work of all, that by Cannon. In the meantime there have been other theories, such as those of metabolism and poisoning. Now has come the fairly fixed theory of the psychogenic causes of the psychoneuroses. Does

the road lead further? There is speculation about such things as vitamins and chemical agents. Physiologists are discussing the differences between humoral and chemical transmission of nerve impulses and are even talking about disease as "chemical disease." It may be necessary to go further into the question. It seems, however, as though the psychogenic basis for the psychoneuroses has become so fixed that one can never get away from it. One may go on, but cannot give up what has already been reached, which seems to be a fundamental point.

CHICAGO NEUROLOGICAL SOCIETY

RICHARD B. RICHTER, M.D., *President, in the Chair*

Regular Meeting, Oct. 19, 1939

EXTRADURAL HEMORRHAGE FROM A TEAR IN THE LATERAL SINUS SIMULATING MIDDLE MENINGEAL HEMORRHAGE: REPORT OF A CASE. DR. HAROLD C. VORIS.

Extradural hemorrhage is usually, but not always, from the middle meningeal artery or one of its branches. At times it may be primarily from torn emissary veins between the bone and the dura. Postoperative extradural hemorrhage is almost invariably from this source. Hemorrhage from a torn dural venous sinus following a depressed fracture of the skull occasionally occurs, but the diagnosis is not difficult if the fracture and its relation to a dural sinus are recognized.

Injury of a dural sinus without depressed fracture is rare. In the only case that I have seen the condition simulated a middle meningeal hemorrhage. In this case a 22 year old white man had fallen from a truck about 4 p. m. on Jan. 3, 1939. He was admitted to the neurosurgical service of the Cook County Hospital an hour later. At the time of admission he was restless and uncooperative, but responded to questions and seemed rational and oriented. The rectal temperature was 98 F., the pulse rate 68, the respiratory rate 16 and the blood pressure 140 systolic and 76 diastolic. He was bleeding profusely from the right ear; there was dried blood in the nostrils, and he occasionally spat blood. There was considerable discoloration behind the right ear. There were swelling of both the frontal and the occipital regions on the right side and discoloration about both orbits. The pupils were small and reacted sluggishly to light; there were no other neurologic findings.

Four hours later the blood pressure was 194 systolic and 80 diastolic, the pulse rate 60 and the respiratory rate 14; breathing was labored; the right pupil was dilated and reacted poorly. The deep reflexes were increased on the left side, but there was no Babinski sign.

A diagnosis of extracerebral hematoma on the right side, probably extradural and originating from the middle meningeal artery or one of its branches, was made, and the patient was taken to the operating room at 11:40 p. m. With local infiltration with 1 per cent procaine hydrochloride, a burr hole was made in the anterior temporal region above and anterior to the ear. This revealed an extradural clot, which, when the burr hole was enlarged with rongeurs, was seen to be thicker toward the base and posteriorly, obviously not originating from the middle meningeal artery or any of its branches.

Accordingly, the small vertical incision first made in the scalp was extended posteriorly and then inferiorly to make a small horseshoe-shaped flap. The resultant flap of scalp and temporal muscle was reflected downward, and then the temporal bone was rongeured away posteriorly, making a subtemporal decompression of the so-called English type. As the opening in the bone was enlarged, the clot, which covered most of the posterior half of the cerebral hemisphere and

measured about 2 cm. in its thickest part, progressively extruded, and finally its origin was apparent. There was a tear in the lateral sinus, just above the mastoid, which was bleeding furiously. However, this hemorrhage was readily controlled by application of a small piece of muscle. Other oozing was controlled and the wound closed in layers with interrupted silk sutures. Before closure a small nick was made in the dura over the temporal lobe, and the cortex was seen to be contused and edematous. Convulsive seizures had begun before the patient was placed on the operating table and continued throughout the entire procedure, in spite of intramuscular administration of 0.3 grain (0.0195 Gm.) of soluble phenobarbital, repeated twice. The convulsions were generalized, but predominantly on the left side.

When the patient left the operating table, at 12:45 p. m., his condition was poor; the rectal temperature was 105 F., the pulse rate 160 and the respiratory rate 56; breathing was labored; the blood pressure was 90 systolic and 50 diastolic. A liter of 10 per cent dextrose was given intravenously and 20 grains (1.3 Gm.) of aminopyrine rectally. Three hours later the rectal temperature was 102.5 F., the pulse rate 100, the blood pressure 110 systolic and 86 diastolic and the respiratory rate 36.

On the following day the patient was comatose, but he had no apparent paralysis. There were no abnormalities in reflexes, and the pupils were equal. Consciousness was gradually regained, and by the fifth postoperative day the patient responded fairly well and was rational and cooperative. Spinal drainage was performed several times, and the fluid, which at first was bloody and under increased pressure, gradually became normal. On the eighth postoperative day paralysis of the right facial nerve of peripheral type was first noted. This was considered to be a late palsy due to edema of the portion of the facial nerve in the facial canal, and early recovery was expected. However, electrical examination of the facial muscles twenty days after operation revealed a reaction of degeneration. In general convalescence was uneventful after the first week, except for an infection of the upper part of the respiratory tract during the fourth week, which delayed dismissal until the twenty-sixth postoperative day. Galvanic treatments of the right facial muscles were continued in the department of physical therapy for four months. Return of function in these muscles was first noted four months after the injury. This has progressed until the present, and recovery is now almost complete. The patient has been employed since May 2, 1939, and at present is working twelve hours a day. He considers himself perfectly well.

CRANIOPHARYNGIOMA OF THE THIRD VENTRICLE OF THE BRAIN: SURGICAL REMOVAL AND PATHOLOGIC STUDY. DR. HOWARD ZEITLIN and DR. ERIC OLDBERG.

This paper will appear in full in a later issue of the ARCHIVES.

OBITUARY: L. HARRISON METTLER, M.D., 1862-1939.

L. Harrison Mettler, who died on March 20, 1939, was active in the early years of the Chicago Neurological Society, which he joined in 1903. He was born in New York in 1863, was graduated from the Jefferson Medical College in 1886 and taught anatomy and neurology at the Medico-Chirurgical College of Philadelphia until he came to Chicago in 1891. From about 1900 until his retirement from teaching and practice in 1916, he was on the faculty of the College of Physicians and Surgeons (now the University of Illinois College of Medicine) and became head of the department of neurology in 1909. He was neurologist to the Cook County Hospital from 1903 to 1906. He was secretary of the Chicago Neurological Society from 1904 to 1906, vice president in 1907 and president in 1909. There are recorded in the minutes of the society seven papers and case demonstrations by him between 1904 and 1911. In 1905 was published his text-

book, of 989 pages: "A Treatise on Diseases of the Nervous System." In the preface he stated that it was written with the view of presenting the subject of neurology in consonance with the neuron doctrine. In the preface one also finds the statement: "Neurology's hardest problems are in the diagnostic sphere. Given a correct diagnosis, the treatment is generally a very simple affair." He loved to apply principles of anatomy and physiology to clinical neurology. Sherrington and Grasset were his favorite authorities. He wrote many papers and always stressed the importance of keeping close to anatomy and physiology. He said that a neurologist not versed in these subjects is like an astronomer ignorant of mathematics, that physiology is the foundation of medicine.

Mettler was a cultured gentleman, with a passionate love for music and poetry. Milton's "Paradise Lost" he read again and again, and he had in his home one of the finest libraries of organ music in the country. He more and more sought seclusion with his books and music and withdrew from the tussle and disharmonies of medical practice. He retired in 1916, at the early age of 53, and spent his remaining twenty-three years in the pursuits he loved most.

OBITUARY: ALBERT BERNARD YUDELSON, M.D. 1872-1939. DR. THEODORE T. STONE.

Albert Bernard Yudelson was born in Suwalki, Poland, on Aug. 2, 1872. His early education was obtained at the Suwalki Gymnasium, from which he graduated in 1892. At this time he was ordained a rabbi. He came to the United States in 1892. From that time until 1896 he was principal of a Hebrew Free School in Troy, N. Y. He was founder of the Nathan and Miriam Barnert Memorial Hebrew Free School in Paterson, N. J., and from 1896 to 1900 was its principal. From 1900 to 1902 he was superintendent of the Hebrew Educational Society of Brooklyn. In 1902 he received the equivalent of the degree of Bachelor of Arts from the regents of the University of the State of New York. He then came to Chicago, and although his chief previous interest had been that of Jewish education, he matriculated at Northwestern University Medical School, graduating in the class of 1906.

In 1908 he was appointed a clinical assistant in the department of nervous and mental diseases at Northwestern University Medical School. In 1914 he was appointed instructor, in 1917 associate, in 1920 assistant professor and in 1925 associate professor, a rank he held until his death. In 1913 he became an adjunct in neurology at Wesley Memorial Hospital. He was attending neurologist to the Provident Hospital from 1913 to 1922. Dr. Yudelson was rabbi of the South Side Hebrew Congregation of Chicago for twelve years. He also founded the Jewish Educational Centre of Chicago in 1915 and served as its president for three years. From 1912 to 1915 he was an associate in neuropsychiatry at the Chicago House of Correction.

Dr. Yudelson served in the World War from April 6, 1918 to March 26, 1919, when he was honorably discharged while at Camp Dix, N. J. He was with the American Expeditionary Forces in France as one of the neuropsychiatrists to Base Hospital no. 62. In July 1920 he was appointed attending specialist in neuropsychiatry of the United States Veterans Bureau for the Eighth district for three years.

From 1926 to 1932 Dr. Yudelson was attending neurologist at the Cook County Hospital. He was a member of the following organizations: the American Medical Association; the Chicago Neurological Society (past president and secretary); the Central Neuropsychiatric Association; the Chicago Society of Internal Medicine; the American College of Physicians; the Association for the Study of Internal Secretions and Phi Delta Epsilon. He also was one of the founders and member of the board of directors of the Jewish People's Institute of Chicago.

His publications dealt with polyuria accompanying lesions of the pituitary body, schizophrenia, the myopathies, facial diplegia in multiple neuritis, mental con-

ditions associated with diseases of the brain and cranial nerves of special sense, and medicolegal studies.

He married Lillian Lapat, daughter of Eliezar and Hannah Lapat, of Paterson, N. J., on June 19, 1921, in Brooklyn.

Dr. Yudelson was a kindly man. He was always willing and ready to assist any one in need of help. He was a friend of the students and was liked by them all. He guided and advised them. His long association with the science of religion created in him a loyal and tolerant personality, which was helpful to his patients. He was respected by his colleagues, with whom he was always friendly.

From 1933 he was either confined at home or at the hospital because of thyrotoxicosis and bilateral cataractous lens. He withstood operations on the thyroid and cataracts, but was unable to resume his work because of anginal attacks. He died in Chicago on Aug. 27, 1939 of coronary thrombosis, at the age of 67.

Book Reviews

Intracranial Tumors of Infancy and Childhood. By Percival Bailey, M.D., with the collaboration of D. N. Buchanan, M.D., and Paul C. Bucy, M.D. Price, $5. Pp. 598. Chicago: University of Chicago Press, 1939.

This stimulating and much needed book is a treasure house of pathologic and clinical knowledge, and is therefore of essential value to the neurologist, pathologist and pediatrician alike. The senior author has devoted twenty years' intelligent observation to the subject, and this has been supplemented and reenforced by the alert assistance of his junior collaborators.

As a background, it should be kept in mind that for ten years Bailey had charge of the Cushing pathologic material, and was able to follow in detail not only the clinical correlations of this finest of all collections but also the manner in which children differ from adults. To this previously acquired knowledge he has added, with the help of Buchanan and Bucy, 100 cases in which the ages of the patients antedated the sixteenth birthday and with the clinicopathologic aspects of which he has dealt in the last ten years. As might be expected of the original and well ordered mind which has provided the modern fundamental classification of tumors of the brain, this latest book also pioneers in throwing into accurate relief the nature of intracranial neoplasms in the young.

The book does more. It evolves a clinical and surgical philosophy, based on this sound and brilliantly erudite pathologic foundation. It takes issue fearlessly with others, but always in a straightforward, honest way, which robs it of maliciousness and gives it personality. If a reviewer were to attempt an epitomization, it might best be done by quoting the final sentence of chapter 14: "When we feel depressed we get back the patients who had astrocytomas and look at them until our spirits rise and we are encouraged to continue the fight against this curse of mankind." Epitomes are dangerous, however, for, like all generalizations, they leave out the qualifications, the details of light and shading and the intangible sense of participation by the reader as he struggles with the authors toward the final intellectual concept.

There is a fitting dedication to Harvey Cushing.

Babies Are Human Beings. By C. Anderson Aldrich and Mary M. Aldrich. Price $1.75. Pp. 128, with 5 illustrations. New York: The Macmillan Company, 1938.

Agreeing that the baby is a psychobiologic unit whose "physical, mental and emotional" growth cannot be considered separately, Drs. Aldrich and Aldrich see him confronted with a world which, as soon as he is born, applies pressure and demands, "taboos and standards" that make his adjustment difficult and thwart his natural growth. Stating that it is their desire to concern themselves with those environmental obstacles that are related to routine training, the authors, in their charming, readable style, outline the physiologic development of the baby's senses through which he is confronted with the world.

Continuing with the clarity that makes this book popular in the layman's library, the authors show in graphically descriptive language the progressive integration of the infant's response to his environment. They point out that a baby can satisfactorily comply with the demand made on him only if his growth has progressed sufficiently to make possible an adequate response. Pliability in management and recognition of individual differences in babies are urged in an effort to blast the popular theory of "standardized" infant-rearing routine. In discussion first of the baby's way of eating, then of sleeping and finally of eliminating, the wide range of variation in these behaviors is illustrated.

The Aldriches have done good work in individualizing the infant, and the book has orienting value not only to parents but also to those in the medical profession

working with children. However, there is a disappointing lack in the book, despite an occasional glimpse that the authors are aware of its importance: that is the lack of emphasis on the psychologic and emotional needs and variations as they are related to the biologic processes so exclusively treated here.

Les embolies cérébrales. By M. Villaret and R. Cachera. Paper. Price, 32 francs. Pp 134, with illustrations. Paris: Masson & Cie, 1939.

This monograph presents the results of a series of experiments concerning cerebral embolism with small particles, observed by means of the Forbes window technic. Powdered glass wool was used as an embolic agent in most of the experiments, and the particles were of a size to obstruct arterioles, or larger. Other mineral particles, and in one series of experiments gaseous emboli, were employed. The pial circulation was studied in some animals during the injection of particles, in others at intervals up to several months afterward.

Embolism with small particles demonstrates clearly the anastomosis of arteries in the pia. In many experiments no parenchymal lesions were produced. The collateral blood vessels around an obstruction dilated, and the region became cyanotic. Further, this method of study showed that local vasoconstriction is readily produced by the mechanical irritation of solid emboli. (The authors were aware that the mineral particles which they employed are more irritating than organic material.) Not only local vasoconstriction results, but the entire arterial network of the region may become subject to scattered intermittent spasms for months after the original impulse. Such spasms may coexist or alternate with vascular dilatation and diapedesis, giving rise to a "moniliform" appearance of the affected arterial tree. In these regions, the capillary circulation becomes congested.

Gaseous emboli may arrest circulation, but they apparently never produce vasoconstriction. The area obstructed, however, is usually much greater than that of infarction by a solid particle, around which a certain amount of collateral circulation may develop.

The Measurement of Adult Intelligence. By David Wechsler. Price, $3.50. Pp. 229, with 40 tables and 12 illustrations. Baltimore: The Williams & Wilkins Company, 1939.

This volume contains a presentation of the Bellevue scale of adult intelligence. Part I discusses the nature and classification of intelligence and the concepts of mental age, the intelligence quotient and mental deficiency and indicates the need for an adult scale of intelligence standardized with adults, thus eliminating the use of children's scales for adults. Part II describes the Bellevue intelligence scale, the selection of the tests that comprise it and their standardization. Part III is a manual of instructions for giving and scoring the tests. This is a clear presentation of problems of measurement of intelligence, and provides a scale which is simple to give and is reliable, being based on a careful statistical analysis of the responses of more than 2,000 clinic subjects.

CORRECTION

Dr. George W. Forman wishes to call attention to errors appearing in his article entitled "Dementia Paralytica: Effect of Continuous Intensive Therapy with Tryparsamide and Bismuth on Cerebrospinal Serologic Reactions and Frequency of Relapse," in the December issue (ARCH. NEUROL. & PSYCHIAT. **42:** 1068, 1939). On page 1072, in line 10, "18.3 per cent" should read "8.3 per cent." On page 1073, in line 20, "16.7 per cent" should read "22.7 per cent;" in line 25, "28.7 per cent" should read "18.7 per cent" and "16.3 per cent" should read "26.3 per cent," and in line 26, "15.1 per cent" should read "25.1 per cent."